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(71) Applicant (for all designated States except US): THE REGENTS OF THE UNIVERSITY OF CALIFORNIA [US/US]; 12th floor, 1111 Franklin Street, Oakland, CA 94607-5200 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): SCANLAN, Thomas, S. [US/US]; 2525 Moraga Street, San Francisco, CA 94122 (US). BAXTER, John, D. [US/US]; 131 San Pablo Avenue, San Francisco, CA 94127 (US). FLETTERICK, Robert, J. [US/US]; 15 Christopher Avenue, San Francisco, CA 94131 (US). WAGNER, Richard, L. [US/US]; 1701 Waller Street, San Francisco, CA 94117 (US). KUSHNER, Peter, J.

[US/US]; 1362 6th Avenue, San Francisco, CA 94122 (US). APRILETTI, James, W. [US/US]; 11 Virginia Gardens, Berkeley, CA 94702 (US). WEST, Brian, L. [US/US]; 142 Anderson Street, San Francisco, CA 94110 (US). SHIAU, Andrew, K. [US/US]; 34 Hugo Street #3, San Francisco, CA 94122 (US).

(74) Agents: BRADBURNE, James, A.; Cooley Godward LLP, 3000 El Camino Real, Five Palo Alto Square, Palo Alto, CA 94306-2155 (US) et al.

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(54) Title: NUCLEAR RECEPTOR LIGANDS AND LIGAND BINDING DOMAINS

(57) Abstract

The present invention provides new methods, particularly computational methods, and compositions for the generation of nuclear receptor synthetic ligands based on the three dimensional structure of nuclear receptors, particularly the thyroid receptor (herein referred to as 'TR'). Also provided are crystals, nuclear receptor synthetic ligands, and related methods.

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NUCLEAR RECEPTOR LIGANDS AND LIGAND BINDING DOMAINS

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CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of the following provisional applications:

10 United States Ser. No. 60/008,540 and 60/008,543, filed December 13, 1995, and Ser.

No. 60/008,606, filed December 14, 1995. This application claims the benefit of the following U.S. patent application: United States Ser. No. 08/764,870, filed December 13, 1996.

INTRODUCTION

Technical Field

This invention relates to computational methods for designing ligands that bind to nuclear receptors, crystals of nuclear receptors, synthetic ligands of nuclear receptors and methods of using synthetic ligands.

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Background

Nuclear receptors represent a superfamily of proteins that specifically bind a physiologically relevant small molecule, such as hormone or vitamin. As a result of a molecule binding to a nuclear receptor, the nuclear receptor changes the ability of a cell to transcribe DNA, i.e. nuclear receptors modulate the transcription of DNA, although they may have transcription independent actions. Unlike integral membrane receptors and membrane associated receptors, the nuclear receptors reside in either the cytoplasm or nucleus of eukaryotic cells. Thus, nuclear receptors comprise a class of intracellular, soluble ligand-regulated transcription factors.

Nuclear receptors include receptors for glucocorticoids (GRs), androgens (ARs), mineralocorticoids (MRs), progestins (PRs), estrogens (ERs), thyroid hormones (TRs), vitamin D (VDRs), retinoids (RARs and RXRs), peroxisomes (XPARs and PPARs) and icosanoids (IRs). The so called "orphan receptors" are also

part of the nuclear receptor superfamily, as they are structurally homologous to the classic nuclear receptors, such as steroid and thyroid receptors. To date, ligands have not been identified with orphan receptors but it is likely that small molecule ligands will be discovered in the near future for this class of transcription factors. Generally, nuclear receptors specifically bind physiologically relevant small molecules with high affinity and apparent Kd's are commonly in the 0.01 - 20 nM range, depending on the nuclear receptor/ligand pair.

Development of synthetic ligands that specifically bind to nuclear receptors has been largely guided by the trial and error method of drug design despite the importance of nuclear receptors in a myriad of physiological processes and medical conditions such as hypertension, inflammation, hormone dependent cancers (e.g. breast and prostate cancer), modulation of reproductive organ function, hyperthyroidism, hypercholesterolemia and obesity. Previously, new ligands specific for nuclear receptors were discovered in the absence of information on the three dimensional structure of a nuclear receptor with a bound ligand. Before the present invention, researchers were essentially discovering nuclear receptor ligands by probing in the dark and without the ability to visualize how the amino acids of a nuclear receptor held a ligand in its grasp.

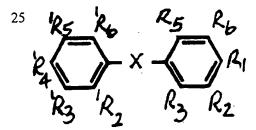
Consequently, it would be advantageous to devise methods and compositions 20 for reducing the time required to discover ligands to nuclear receptors, synthesize such compounds and administer such compounds to organisms to modulate physiological processes regulated by nuclear receptors.

SUMMARY OF THE INVENTION

The present invention provides for crystals of nuclear receptor ligand binding domains with a ligand bound to the ligand binding domain (LBD). The crystals of the present invention provide excellent atomic resolution of the amino acids that interact 5 with nuclear receptor ligand, especially thyroid receptor ligands. The three dimensional model of a nuclear receptor LBD with a ligand bound reveals a previously unknown structure for nuclear receptors and shows that the ligand is bound in a water inaccessible binding cavity of the ligand binding domain of the nuclear receptor.

The present invention also provides for computational methods using three dimensional models of nuclear receptors that are based on crystals of nuclear receptor LBDs. Generally, the computational method of designing a nuclear receptor ligand determines which amino acid or amino acids of a nuclear receptor LBD interact with a chemical moiety (at least one) of the ligand using a three dimensional model of a crystallized protein comprising a nuclear receptor LBD with a bound ligand, and selecting a chemical modification (at least one) of the chemical moiety to produce a second chemical moiety with a structure that either decreases or increases an interaction between the interacting amino acid and the second chemical moiety compared to the interaction between the interacting amino acid and the corresponding 20 chemical moiety on the natural hormone.

Also provided is a method of modulating the activity of a nuclear receptor. The method can be *in vitro* or *in vivo*. The method comprises administering *in vitro* or *in vivo* a sufficient amount of a compound of the following formula:



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FORMULA I.

where the compound fits specially and preferentially into a nuclear hormone receptor LBD of interest. The method is exemplified by modulating the activity of a thyroid receptor (TR). For modulating TR activity, a compound of Formula I is employed

that fits spacially and preferentially into a TR ligand binding domain (TR LBD), including compounds specific for a TR LBD isoform of interest. Of particular interest are the TR LBD isoforms α (TR-α) and β (TR-β). Additional compounds of interest include derivatives of Formula I, such as those compounds having the biphenyl (φ-X-5 φ) or single phenyl (φ-X or X-φ) nucleus of Formula I and its corresponding substituent groups described herein. Compounds that are interatively designed using structural information gleaned from these compounds and which modulate nuclear hormone receptor activity also are of interest.

The present invention also includes a method for identifying a compound capable of selectively modulating the activity of a nuclear receptor. This aspect of the invention is exemplified by a method for identifying a compound capable of selectively modulating the activity of a TR isoform. The method comprises modeling test compounds that fit spacially and preferentially into a TR LBD isoform of interest using an atomic structural model of a TR LBD isoform bound to a test compound, screening the test compounds in a biological assay for TR isoform activity characterized by binding of a test compound to a TR LBD isoform, and identifying a test compound that selectively modulates the activity of a TR isoform. The compounds may be those of Formula I or derivatives thereof, including compounds having a biphenyl or single phenyl nucleus of Formula I.

Purther included is a method for identifying agonist or antagonist ligands of a nuclear receptor using the atomic coordinates of a LBD in conjunction with a computerized modeling system. This aspect of the invention is exemplified by identifying a TR agonist or antagonist ligand by providing the atomic coordinates of a TR LBD to a computerized modeling system, modeling ligands which fit spacially into the TR LBD, and identifying in a biological assay for TR activity a ligand which increases or decreases TR activity. The compounds can be those of Formula I or derivatives thereof, including compounds having a biphenyl or single phenyl nucleus of Formula I.

Also provided is a method of identifying a compound that selectively 30 modulates the activity of one type of nuclear receptor compared to other nuclear hormone receptors. The method is exemplified by modeling test compounds which fit spacially into a TR LBD using an atomic structural model of a TR LBD, selecting a compound comprising conformationally constrained structural features that interact

with conformationally constrained residues of a TR LBD, and identifying in a biological assay for TR activity a compound that selectively binds to a TR LBD compared to other nuclear receptors. The conformationally constrained features involved in receptor-selective ligand binding can be identified by comparing atomic 5 models of receptor isoforms bound to the same and/or different ligands. The methods facilitate design and selection of compounds that have increased selectivity for a particular nuclear receptor. The compounds may be those of Formula I or derivatives thereof, including compounds having the biphenyl or single phenyl nucleus of Formula I.

Another aspect of the invention is a method for increasing the receptor selectivity of a compound for a particular type of nuclear receptor. This involves the chemical modification of a substituent group of a compound of Formula I to generate compounds which have increased selectivity for one type of receptor. For example, chemical modification of a substituent group of the compound of Formula I can be used to introduce additional constraints into a compound that modulates TR activity to increase its selectivity in vivo for TR-type receptors. Additional constraints also may be added for stability. The modified groups will preferably interact with a conformationally constrained structural feature of a TR LBD that is conserved among TR isoforms. A more preferred method comprises selecting compounds having conformationally constrained groups that interact with conformationally constrained residues of a TR LBD conserved among TR isoforms. The compounds can be those of Formula I or derivatives thereof, including compounds having the biphenyl or single phenyl nucleus of Formula I.

The invention finds use in the selection and characterization of peptide, 25 peptidomimetic or synthetic compounds identified by the methods of the invention, particularly new lead compounds useful in treating disorders related to nuclear receptor-based deficiencies, including TR-related disorders. For TR-related disorders, the compounds and methods of the invention can be used to modulate TR activity by administering to a mammal in need thereof a sufficient amount of compound of 30 Formula I or derivative thereof that fits spacially and preferentially into a TR LBD.

BRIEF DESCRIPTION OF THE DRAWINGS

- FIG. 1 is a diagram illustrating computational methods for designing ligands that interact with nuclear receptors of the nuclear receptor superfamily.
- FIG. 2 is a schematic representation of nuclear receptor structures, indicating 5 regions of homology within family members and functions of the various domains.
 - FIG. 3 shows the aligned amino acid sequences of the ligand binding domains of several members of the nuclear receptor superfamily.
- FIG. 4 is a ribbon drawing of the rat TR-α LBD with secondary structure elements labelled. The ligand (magenta) is depicted as a space-filling model. Alpha 10 helices and coil conformations are yellow, beta strands are blue.
 - FIG. 5 shows two cross-sections of a space-filling model of rat $TR-\alpha$ exposing the ligand (magenta) tightly packed within the receptor.
- FIG. 6 is a schematic of the ligand binding cavity. Residues which interact with the ligand appear approximately at the site of interaction. Hydrogen bonds are shown as dashed lines between the bonding partners; distances for each bond are listed. Non-bonded contacts are shown as radial spokes which face toward interacting atoms.
- FIG. 7 is the distribution of crystallographic temperature factors in the refined rat TR-I LBD. The distribution is represented as a color gradation ranging from less 20 than 15 (dark blue) to greater than 35 (yellow-green).
- FIG. 8 is a ribbon drawing of the rat TR-α LBD showing the c-terminal activation domain to ligand. Residues which comprise the c-terminal activation domain (Pro393-Phe405) are depicted as a stick representation. Hydrophobic residues, particularly Phe401 and Phe405 (blue) face inwards toward the ligand.

 25 Glu403 (red) projects outward into the solvent.
 - FIG. 9 is an electrostatic potential surface of the rat TR- α LBD, calculated using GRAPH. Negative electrostatic potential is red; positive electrostatic potential is blue. The c-terminal activation domain forms a largely hydrophobic (white). The Glu403 is presented as a singular patch of negative charge (red).
- FIG. 10 is a diagram comparing agonists and antagonists for several nuclear receptors.
 - FIG. 11 is the synthetic scheme for preparation of TS1, TS2, TS3, TS4 and TS5.

FIG. 12 is the synthetic scheme for preparation of TS6 and TS7.

- FIG. 13 is the synthetic scheme for preparation of TS8.
- FIG. 14 is the synthetic scheme for preparation of TS10.
- FIG. 15 depicts the chemical structures of several TR ligands.
- 5 FIG. 16 is a graph illustrating competition assays in which T₃ and Triac compete with labeled T₃ for binding to human TR-α or human TR-β.
 - FIG. 17 depicts a Scatchard analysis of labelled T₃ binding to TR-α and TR-β.
- FIG. 18 is a chart showing the effect of TS-10 on the transcriptional regulation of the DR4-ALP reporter gene in the presence or absence of T3 as assayed 10 in TRAFI1 reporter cells.
 - FIG. 19 is a chart showing the effect of TS-10 on the transcriptional regulation of the DR4-ALP reporter gene in the presence or absence of T3 as assayed in TRAF91 reporter cells.
- FIG. 20 is a chart showing the effect of TS-10 on the transcriptional 15 regulation of the DR4-ALP reporter gene in the presence or absence of T3 as assayed in HepG2, a liver reporter cell line.
 - FIG. 21 is a partial ribbon drawing of TR-α LBD with T3 in the ligand binding cavity. Selected interacting amino acids are labelled, including Ile221, Ile222 and Ser260, Ala263, Ile299 and Leu 276.
- FIG. 22 is a partial ribbon drawing of TR-α LBD with T3 and Dimit superimposed in the ligand binding cavity. Interactions with Ile221, Ile222, Ala260, Ile 299 and Leu276 are labelled.
- FIG. 23 is a partial ribbon drawing of TR-α LBD with T3, illustrating the three Arginine residues (Arg228, Arg262 and Arg 266 (dark stick figures)) of the polar pocket, three water molecules HOH502, HOH503 and HOH504, with hydrogen bonds indicated by dotted lines.
 - FIG. 24 is a partial ribbon drawing of TR-α LBD with Triac, illustrating the three Arginine residues (dark stick figures) of the polar pocket, water molecules (HOH503, HOH504 and HOH600), with hydrogen bonds indicated by dotted lines.
- FIG. 25 is a partial ribbon drawing of the TR-α LBD with T3 and Triac superimposed in the ligand binding cavity. The drawing shows several interacting amino acid residues in the polar pocket that remain unchanged whether T3 or Triac occupies the ligand binding cavity: Arg262, Asn179, HOH503 and HOH504, and

Ser277. Both Arg228 and Arg 266 occupy two different positions, depending on whether T3 or Triac is bound.

- FIG. 26A and 26B are stereochemical representations of the TR- α LBD with Dimit bound.
- FIG. 27 is a partial ribbon drawing of TR-β LBD with GC-1 in the ligand binding cavity. Amino acids Arg282, Arg316, Arg320, Asn 331 and His435 are labelled.
- FIG. 28 is a partial ribbon drawing of TR-β LBD with Triac in the ligand binding cavity. Amino acids Arg282, Arg316, Arg320, Asn331 and His435 are 10 labelled.
 - FIG. 29 is a partial ribbon drawing of TR-βLBD with GC-1 (Blue) overlayed with TR-α LBD with Dimit (Red) in the ligand binding cavities. Amino acids Arg228, Arg262, Arg266 and Ser277 (TR-α LBD), and Arg282, Arg316, Arg320 and Asn331 (TR-β LBD) are labelled.
- FIG. 30 is a partial ribbon drawing of TR-β LBD with Triac (Blue) overlayed with TR-α LBD with Triac (Red) in the ligand binding cavities. Amino acids Arg228, Arg262, Arg266, Ser277 and His381 (TR-α LBD), and Arg282, Arg316, Arg320 and His435 (TR-β LBD) are labelled.
- FIG. 31 is a graph showing competition curves comparing wildtype TR-α and 20 TR-β to a variant TR-β having a single amino acid substitution in the ligand binding domain.
 - FIG. 32 shows atomic numbering for thyronine-like ligands.
 - **APPENDIX 1** is an appendix of references.
- APPENDIX 2 is a chart of amino acids that interact with a TR ligand, for TR 25 complexed with Dimit, Triac, IpBr2, T3 and GC-1.
 - APPENDIX 3 is a chart of atomic coordinates for the crystal of rat $TR-\alpha$ LBD complexed with Dimit.
 - APPENDIX 4 is a chart of atomic coordinates for the crystal of rat $TR-\alpha$ LBD complexed with Triac.
- APPENDIX 5 is a chart of atomic coordinates for the crystal of rat TR-α LBD complexed with IpBr₂.

APPENDIX 6 is a chart of atomic coordinates for the crystal of rat $TR-\alpha$ LBD complexed with T_3 .

APPENDIX 7 is a chart of atomic coordinates for the crystal of human TR- β LBD complexed with Triac.

5 APPENDIX 8 is a chart of atomic coordinates for the crystal of human TR-β-LBD complexed with GC-1.

DETAILED DESCRIPTION OF THE INVENTION

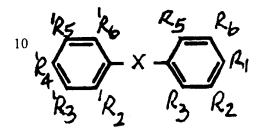
INTRODUCTION

The present invention provides new methods, particularly computational methods, and compositions for the generation of nuclear receptor synthetic ligands based on the three dimensional structure of nuclear receptors, particularly the thyroid receptor (herein referred to as "TR"). Previously, the lack of three dimensional structural information about the ligand binding domain of a nuclear receptor thwarted the field of nuclear receptor drug discovery, especially the absence of three dimensional structural information relating to a nuclear receptor with a ligand bound.

Described herein for the first time are crystals and three dimensional structural information from a nuclear receptor's ligand binding domain (LBD) with a ligand bound. The structure of the TR LBD complexed with 3,5,3'-triiodothyronine (T₃), 20 3,5-dibromo-3'-isopropylthyronine (IpBr₂), 3,5- dimethyl-3'-isopropylthyronine (Dimit), and 3,5,3'-triiodothyroacetic acid (Triac), 3,5-dimethyl-4-(4'-hydroxy-3'isopropylbenzyl)-phenoxy acetic acid (GC1) are exemplified. Such crystals offer superior resolution at the atomic level and the ability to visualize the coordination of nuclear receptor ligands by amino acids that comprise the LBD. The present 25 invention also provides computational methods for designing nuclear receptor synthetic ligands using such crystal and three dimensional structural information to generate synthetic ligands that modulate the conformational changes of a nuclear receptor's LBD. Such synthetic ligands can be designed using the computational methods described herein and shown, in part, in FIG. 1. These computational 30 methods are particularly useful in designing an antagonist or partial agonist to a nuclear receptor, wherein the antagonist or partial agonist has an extended moiety that prevents any one of a number of ligand-induced molecular events that alter the receptor's influence on the regulation of gene expression, such as preventing the

normal coordination of the activation domain observed for a naturally occurring ligand or other ligands that mimic the naturally occurring ligand, such as an agonist. As described herein, synthetic ligands of nuclear receptors will be useful in modulating nuclear receptor activity in a variety of medical conditions.

Of particular interest is use of such ligands in a method of modulating TR activity in a mammal by administering to a mammal in need thereof a sufficient amount of a compound of Formula I,



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where the compound fits spatially and preferentially into a TR LBD. By "fits spacially" is intended that the three-dimensional structure of a compound is accommodated geometrically by a cavity or pocket of a TR LBD. By "TR LBD" is intended a structural segment or segments of thyroid hormone receptor polypeptide 20 chain folded in such a way so as to give the proper geometry and amino acid residue configuration for ligand binding. This is the physical arrangement of protein atoms in three-dimensional space forming a ligand binding pocket or cavity. By "fits spacially and preferentially" is intended that a compound possesses a three-dimensional structure and conformation for selectively interacting with a TR LBD. Compounds of 25 interest also include derivatives of Formula I. By "derivatives of Formula I" is intended compounds that comprise at least a single phenyl scaffold (φ-X or X-φ) of the biphenyl scaffold (\(\phi - \text{X} - \phi \)) of Formula I which comprise the corresponding substituents of Formula I described herein. Compounds that are interatively designed using structural information gleaned from these compounds and which 30 modulate nuclear hormone receptor activity also are of interest. Preferred compounds of Formula I and its derivatives that fit spacially and preferentially into a TR LBD comprise the following substituents:

(i) an R1-substituent comprising an anionic group that interacts with a side chain nitrogen atom of an arginine corresponding to a residue from the group Arg228, Arg262, and Arg266 of human TR-α, and Arg282, Arg316 and Arg320 of human TR-β, where the anionic group is about 1.7-4.0Å from the nitrogen atom;

- 5 (ii) an R2-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- (iii) an R3-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a serine, alanine and/or isoleucine corresponding to a residue from the group Ser260, Ala263 and Ile299 of human TR-α, and Ser314,
 10 Ala317 and Ile352 of human TR-β, where the hydrophobic or hydrophilic group is about 1.7-4.0Å from the side chain atom:
- (iv) an R5-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a phenylalanine and/or isoleucine corresponding to a residue from the group Phe218, Ile221 and Ile222 of human TR-α, and Phe272,
 15 Ile275 and Ile276 of human TR-β, where the hydrophobic or hydrophilic group is about 1.7-4.0Å from the side chain atom;
 - (v) an R6-substitutent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- (vi) an X-substituent comprising a hydrophobic or hydrophilic group that 20 interacts with a side chain atom of a leucine corresponding to a residue from the group Leu276 and Leu292 of human TR-α, and Leu 330 and Leu346 of human TR-β, where the hydrophobic or hydrophilic group is about 1.7-4.0Å from the side chain atom;
- (vii) an R2'-substituent comprising a hydrophobic or hydrophilic group that 25 fits spacially into the TR LBD;
- (viii) an R3'-substituent comprising a hydrophobic group that interacts with a side chain atom of a phenylalanine, glycine and/or methionine corresponding to a residue from the group Phe215, Gly290, and Met388 of human TR-α, and Phe269, Gly344, Met442 of human TR-β, where the hydrophobic group is about 1.7-4.0Å 30 from the side chain atom:
 - (ix) an R4'-substituent comprising an hydrogen bond donor or acceptor group that interacts with a side chain carbon or nitrogen atom of a histidine corresponding to residue His381 of human TR-α, and His435 of human TR-β, where

the hydrogen bond donor or acceptor group is about 1.7-4.0Å from the side chain atom;

- (x) an R5'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- 5 (xi) and R6'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD; and

where the compound is other than thyronine (T3), triiodothyronine (T4) or other thyronine-like compounds previously known and used in a TR treatment method, such as those referenced in Appendix I.

10 Examples of such substituents include the following: where R_1 is

-CH₂CH[NH-tBOC]CO₂H, or a carboxylate connected to the ring with a 0 to 3 carbon linker,

-PO₃H₂, -CH₂PO₃H₂, -CH₂CH₂PO₃H₂, -CH₂CHNH₂PO₃H₂, -CH₂CH[NHCOCH ϕ_2]PO₃H₂, -CH₂CH[NHCO(CH₂)₁₅CH₃]PO₃H₂,

-CH₂CH[NH-FMOC]PO₃H₂, -CH₂ CH[NH-tBOC]PO₃H₂, or a phosphate or phosphonate connected to the ring with a 0 to 3 carbon linker,

-SO₃H, -CH₂SO₃H, -CH₂CH₂SO₃H, -CH₂CH[NHCO(CH₂)₁₅CH₃]SO₃H, -CH₂CH[NHCO(CH₂)₁₅CH₃]SO₃H,

-CH₂CH[NH-FMOC]SO₃H, -CH₂ CH[NH-tBOC]SO₃H, or a sulfate or sulfite

connected to the ring with a 0 to 3 carbon linker, or acts as the functional equivalent of CH₂CH(NH₂)CO₂H of T3 in the molecular recognition domain

when bound to a TR, wherein R₁ can be optionally substituted with an amine,

where R₂ is

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H, halogen, CF₃, OH, NH₂, SH, CH₃, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

30 where R₃ is

-H, halogen, -CF₃, -OH, -NH₂, -N₃, -SH, -CH₃, -Et, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR, where R_5 is

-H, halogen, -CF₃, -OH, -NH₂, -N₃, -SH, -CH₃, -Et, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR, and R_3 can be identical to R_5 ,

where R₆ is

5 -H, halogen, -CF₃, -OH, -NH₂, -SH, -CH₃, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR, and R₂ can be identical to R₆,

where R2' is

-H, halogen, -CF₃, -OH, -NH₂, -N₃, -SH, -CH₃, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

where R₃' is any hydrophobic group, including

halogen, -CF₃, -SH, alkyl, aryl, 5- or 6-membered heterocyclie, cyano, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR,

15 where R₄' is

-H, halogen, -CF₃, -OH, -NH₂, NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate or sulfate, -SH, -CH₃, -Et, or akyl, aryl or 5- or 6-membered heterocyclic aromatic attached through urea or carbamate linkages to O or N or S at the R₄' position, or acts as the functional equivalent of OH in the molecular recognition domain when bound to a TR,

where R₅' is

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-H, -OH, -NH₂, -N(CH₃)₂ -SH -NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate, sulfate, branched or straight chain alkyl having 1 to 9 carbons, substituted or unsubstituted aryl, wherein said substituted aryl is substituted with halogen or 1 to 5 carbon alkyl and wherein said aryl is optionally connected to the ring by a -CH₂-, aromatic heterocycle having 5 to 6 atoms, wherein said heterocycle may be substituted with one or more groups selected from -OH, -NH₂, -SH, -NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate or sulfate, heteroalkyl, arylalkyl, heteroaryl alkyl, polyaromatic, or polyheteroaromatic, wherein said R₅' may be substituted with polar or charged groups,

where R₆' is

-H, halogen, -CF₃, -OH, -NH₂, -SH, -CH₃, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

where X is

O, S, SO₂, NH, NR₇, CH₂, CHR₇, CR₇R₇, wherein R₇ is alkyl, aryl or 5- or 6-membered heterocyclic aromatic,

and where the TR LBD ligand has an apparent Kd for binding TR LBD of 1 TM or 5 less.

Of particular interest are the class of compounds according to Formula I having the following substituents: where R₁ is carboxylate, phosphonate, phosphate or sulfite and is connected to the ring with a 0 to 3 carbon linker, R₂ is H, R₃ is -I, -Br, or -CH₃, R₅ is -I, -Br, or -CH₃, R₆ is H, R₂' is H, R₃' is -I, -Br, -CH₃, -iPr, -phenyl, 10 benzyl, or 5- or 6-membered ring heterocycles, R₄' is -OH, -NH₂, and -SH, R₅' is -H, -OH, -NH₂, -N(CH₃)₂ -SH -NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate, sulfate, branched or straight chain alkyl having 1 to 9 carbons, substituted or unsubstituted aryl, wherein said substituted aryl is substituted with halogen or 1 to 5 carbon alkyl and wherein said aryl is optionally connected to the ring by a -CH₂-, 15 aromatic heterocycle having 5 to 6 atoms, wherein said heterocycle may be substituted with one or more groups selected from -OH, -NH₂, -SH, -NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate or sulfate, heteroalkyl, arylalkyl, heteroaryl alkyl, polyaromatic, or polyheteroaromatic, wherein said R₅' may be substituted with polar or charged groups, and R₆' is H.

The present invention also includes a method for identifying a compound 20 capable of selectively modulating the activity of a TR isoform. By "modulating" is intended increasing or decreasing activity of a TR. By "TR isoform" is intended TR proteins encoded by subtype and variant TR genes. This includes TR-α and TR-β isoforms encoded by different genes (e.g., thra and thrb) and variants of the same 25 genes (e.g., thrb1 and thrb2). The method comprises the steps of modeling test compounds that fit spacially and preferentially into a TR LBD isoform of interest using an atomic structural model of a TR LBD isoform bound to a test compound, screening the test compounds in a biological assay for TR isoform activity characterized by binding of a test compound to a TR LBD isoform, and identifying a 30 test compound that selectively modulates the activity of a TR isoform. "modeling" is intended quantitative and qualitative analysis of receptor-ligand structure/function based on three-dimensional structural information and receptor-This includes conventional numeric-based molecular ligand interaction models.

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dynamic and energy minimization models, interactive computer graphic models, modified molecular mechanics models, distance geometry and other structure-based constraint models. Modeling is preferably performed using a computer and may be further optimized using known methods.

For selectively modulating activity of a TR isoform, such as TR-α or TR-β, a sufficient amount of a compound that fits spatially and preferentially into TR LBD isoform is provided *in vitro* or *in vivo* to achieve the desired end result. TR-α isoform selectivity can be accomplished with a compound comprising an anionic group that interacts with an oxygen or carbon of a serine residue corresponding to Ser277 of 10 human TR-α, where the anionic group is about 1.7-4.0Å from the side chain atom. TR-β isoform selectivity can be accomplished with a compound comprising an anionic group that interacts with the side chain nitrogen of an asparagine corresponding to Asn331 of human TR-β, where the anionic group is about 1.7-4.0Å from the side chain nitrogen atom.

The present invention further includes a method for identifying a TR agonist or antagonist ligand by providing the atomic coordinates of a TR LBD to a computerized modeling system, modeling ligands which fit spacially into the TR LBD, and identifying in a biological assay for TR activity a ligand which increases or decreases the activity of the TR.

The invention also involves a method for increasing receptor selectivity of a compound of Formula I or derivatives thereof for a TR-type receptor versus other nuclear receptors by selecting a compound that interacts with conformationally constrained residues of a TR LBD that are conserved among TR isoforms. "Conformationally constrained" is intended to refer to the three-dimensional structure of a chemical or moiety thereof having certain rotations about its bonds fixed by various local geometric and physical-chemical constraints. In designing and selecting compounds having increased specificity for TRs compared to other nuclear receptors, the following methods of the invention can be used. One method involves comparing atomic models of a first TR LBD isoform bound to a compound with a second TR LBD isoform bound to the same compound, identifying atoms of the TR LBD and compounds which interact, and designing or selecting a compound that interacts with TR LBD residues comprising a conformationally constrained structural feature that is conserved between the TR LBD isoforms. Another method relates to comparing a

first TR LBD complexed with a first compound to a second TR LBD complexed with a second compound having one or more different substituents compared to the first compound, identifying atoms of the TR LBD and compounds which interact, and designing or selecting compounds that interact with TR LBD residues comprising a 5 conformationally constrained structural feature that is conserved between the TR LBD isoforms. The methods also facilitate identification of structural and conformationally constrained interactions that are conserved between compounds that bind to a TR LBD. The methods are exemplified by comparing atomic models of a first TR LBD isoform complexed with a first compound of Formula I to a second TR LBD isoform 10 complexed with the first compound, or a second compound of Formula I having different substituents than the first compound. For example, a TR-α LBD bound to a natural hormone such as T3 is compared to a TR-B LBD bound to an organic thyronine-like compound such as GC-1. Conserved contacts are identified which are made between atoms of the different compounds and atoms of the TR LBDs, and the 15 fiducial and adjustable components identified. Compounds selective for TR are identified in a biological assay for TR activity that assays for selective binding to a TR and/or TR LBD compared to other nuclear receptors. Conventional assays for TR and other nuclear receptors may be conducted in parallel or serially, including those assays described herein. Automatable methods are preferred. The methods facilitate 20 design and selection of compounds comprising cyclic carbon and substituent atoms that interact with a constrained side chain and/or main chain atom of a TR LBD residue.

In another aspect of the invention, the methods described herein are useful for selecting peptides, peptidomimetics or synthetic molecules that modulate TR activity.

25 Methods of the invention also find use in characterizing structure/function relationships of natural and synthetic TR-ligands. Molecules of particular interest are new thyronine-like compounds other than T3, T4 and other thyronine-like compounds previously known and used for treating TR-related disorders. New compounds of the invention include those which bind to a TR LBD isoform with greater affinity than T3 or T4 and those which exhibit isoform-specific binding affinity.

APPLICABILITY TO NUCLEAR RECEPTORS

The present invention, particularly the computational methods, can be used to design drugs for a variety of nuclear receptors, such as receptors for glucocorticoids (GRs), androgens (ARs), mineralocorticoids (MRs), progestins (PRs), estrogens 5 (ERs), thyroid hormones (TRs), vitamin D (VDRs), retinoid (RARs and RXRs), icosanoid (IRs), and peroxisomes (XPARS and peroxisomal proliferators (PPAP)). The present invention can also be applied to the "orphan receptors," as they are structurally homologous in terms of modular domains and primary structure to classic nuclear receptors, such as steroid and thyroid receptors. The amino acid homologies 10 of orphan receptors with other nuclear receptors ranges from very low (<15%) to in the range of 35% when compared to rat RARI and human TR-β receptors, for example. In addition, as is revealed by the X-ray crystallographic structure of the TR and structural analysis disclosed herein, the overall folding of liganded superfamily members is likely to be similar. Although ligands have not been identified with 15 orphan receptors, once such ligands are identified one skilled in the art will be able to apply the present invention to the design and use of such ligands, as their overall structural modular motif will be similar to other nuclear receptors described herein.

Modular Functional Domains Of Nuclear receptors

- The present invention will usually be applicable to all nuclear receptors, as discussed herein, in part, to the patterns of nuclear receptor activation, structure and modulation that have emerged as a consequence of determining the three dimensional structures of nuclear receptors with different ligands bound, notably the three dimensional structures or crystallized protein structure of the ligand binding domains for TR-α and TR-β. Proteins of the nuclear receptor superfamily display substantial regions of amino acid homology, as described herein and known in the art see FIG. 2. Members of this family display an overall structural motif of three modular domains (which is similar to the TR three modular domain motif):
 - 1) a variable amino-terminal domain;
- 30 2) a highly conserved DNA-binding domain (DBD); and
 - 3) a less conserved carboxyl-terminal LBD.

The modularity of this superfamily permits different domains of each protein to separately accomplish different functions, although the domains can influence each

other. The separate function of a domain is usually preserved when a particular domain is isolated from the remainder of the protein. Using conventional protein chemistry techniques a modular domain can sometimes be separated from the parent protein. Using conventional molecular biology techniques each domain can usually be separately expressed with its original function intact or chimerics of two different nuclear receptors can be constructed, wherein the chimerics retain the properties of the individual functional domains of the respective nuclear receptors from which the chimerics were generated.

FIG. 2 provides a schematic representation of family member structures,
10 indicating regions of homology within family members and functions of the various domains.

Amino Terminal Domain

The amino terminal domain is the least conserved of the three domains and varies markedly in size among nuclear receptor superfamily members. For example, this domain contains 24 amino acids in the VDR and 603 amino acids in the MR. This domain is involved in transcriptional activation and in some cases its uniqueness may dictate selective receptor-DNA binding and activation of target genes by specific receptor isoforms. This domain can display synergistic and antagonistic interactions with the domains of the LBD. For example, studies with mutated and/or deleted receptors show positive cooperativity of the amino and carboxy terminal domains. In some cases, deletion of either of these domains will abolish the receptor's transcriptional activation functions.

25 DNA-Binding Domain

The DBD is the most conserved structure in the nuclear receptor superfamily. It usually contains about 70 amino acids that fold into two zinc finger motifs, wherein a zinc ion coordinates four cysteines. DBDs contain two perpendicularly oriented I-helixes that extend from the base of the first and second zinc fingers. The two zinc 30 fingers function in concert along with non-zinc finger residues to direct nuclear receptors to specific target sites on DNA and to align receptor homodimer or heterodimer interfaces. Various amino acids in DBD influence spacing between two half-sites (usually comprised of six nucleotides) for receptor dimer binding. For

example, GR subfamily and ER homodimers bind to half-sites spaced by three nucleotides and oriented as palindromes. The optimal spacings facilitate cooperative interactions between DBDs, and D box residues are part of the dimerization interface. Other regions of the DBD facilitate DNA-protein and protein-protein interactions required for RXR homodimerization and heterodimerization on direct repeat elements.

The LBD may influence the DNA binding of the DBD, and the influence can also be regulated by ligand binding. For example, TR ligand binding influences the degree to which a TR binds to DNA as a monomer or dimer. Such dimerization also depends on the spacing and orientation of the DNA half sites. The receptors also can interact with other proteins and function to regulate gene expression.

The nuclear receptor superfamily has been subdivided into two subfamilies: 1) GR (GR, AR, MR and PR) and 2) TR (TR, VDR, RAR, RXR, and most orphan receptors) on the basis of DBD structures, interactions with heat shock proteins (hsp), and ability to form heterodimers. GR subgroup members are tightly bound by hsp in the absence of ligand, dimerize following ligand binding and dissociation of hsp, and show homology in the DNA half sites to which they bind. These half sites also tend to be arranged as palindromes. TR subgroup members tend to be bound to DNA or other chromatin molecules when unliganded, can bind to DNA as monomers and dimers, but tend to form heterodimers, and bind DNA elements with a variety of orientations and spacings of the half sites, and also show homology with respect to the nucleotide sequences of the half sites. By this classification, ER does not belong to either subfamily, since it resembles the GR subfamily in hsp interactions, and the TR subfamily in nuclear localization and DNA-binding properties.

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Ligand Binding Domain

The LBD is the second most highly conserved domain in these receptors. Whereas integrity of several different LBD sub-domains is important for ligand binding, truncated molecules containing only the LBD retain normal ligand-binding activity. This domain also participates in other functions, including dimerization, nuclear translocation and transcriptional activation, as described herein. Importantly, this domain binds the ligand and undergoes ligand-induced conformational changes as detailed herein.

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Most members of the superfamily, including orphan receptors, possess at least two transcription activation subdomains, one of which is constitutive and resides in the amino terminal domain (AF-1), and the other of which (AF-2 (also referenced as TAU 4)) resides in the ligand-binding domain whose activity is regulated by binding 5 of an agonist ligand. The function of AF-2 requires an activation domain (also called transactivation domain) that is highly conserved among the receptor superfamily (approximately amino acids 1005 to 1022). Most LBDs contain an activation domain. Some mutations in this domain abolish AF-2 function, but leave ligand binding and other functions unaffected. Ligand binding allows the activation domain to serve as 10 an interaction site for essential co-activator proteins that function to stimulate (or in some cases, inhibit) transcription.

For example, Shibata, H., et al. (Recent Progress in Hormone Res. 52:141-164 (1997)) has reviewed the role of co-activators and co-repressors in steroid/thyroid hormone receptor systems. Steroid receptor co-activator-one (SRC-1) appears to be a 15 general co-activator for all AF-2 domain containing receptors tested. SRC-1 enhances transactivation of steroid hormone-dependent target genes. Other putative coactivators have been reported, including the SRC-1 related proteins, TIF-2 and GRIP-1, and other putative unrelated co-activators such as ARA-70, Trip 1, RIP-140, and TIF-1. In addition another co-activator CREB-binding protein (CBP) has been shown 20 to enhance receptor-dependent target gene transcription. CBP and SRC-1 interact and synergistically enhance trancriptional activation by the ER and PR. A ternary complex of CBP, SRC-1, and liganded receptors-may form to increase the rate of hormone-responsive gene transcription. Co-repressors, such as SMRT and N-CoR, for TR and RAR, have been identified that also contribute to the silencing function of 25 unliganded TR. The unliganded TR and RAR have been shown to inhibit basal promoter activity; this silencing of target gene transcription by unliganded receptors is mediated by these co-repressors. The collective data suggests that upon binding of agonist, the receptor changes its conformation in the ligand-binding domain that enables recruitment of co-activators, which allows the receptor to interact with the 30 basal transcriptional machinery more efficiently and to activate transcription. In contrast, binding of antagonists induces a different conformational change in the receptor. Although some antagonist-bound receptors can dimerize and bind to their cognate DNA elements, they fail to dislodge the associated co-repressors, which results in a nonproductive interaction with the basal transcriptional machinery.

Similarly, the TR and RAR associate with co-repressors in the absence of ligand, thereby resulting in a negative interaction with the transcriptional machinery that silences target gene expression. In the case of mixed agonist/antagonists, such as 4-hydroxytamoxifen, activation of gene transcription may depend on the relative ratio of co-activators and co-repressors in the cell or cell-specific factors that determine the relative agonistic or antagonistic potential of different compounds. These co-activators and co-repressors appear to act as an accelerator and/or a brake that modulates transcriptional regulation of hormone-responsive target gene expression.

The carboxy-terminal activation subdomain, as described herein is in close three dimensional proximity in the LBD to the ligand, so as to allow for ligands bound to the LBD to coordinate (or interact) with amino acid(s) in the activation subdomain. As described herein, the LBD of a nuclear receptor can be expressed, crystallized, its three dimensional structure determined with a ligand bound (either using crystal data from the same receptor or a different receptor or a combination thereof), and computational methods used to design ligands to its LBD, including ligands that contain an extension moiety that coordinates the activation domain of the nuclear receptor.

Once a computationally designed ligand (CDL) is synthesized as described herein and known in the art, it can be tested using assays to establish its activity as an 20 agonist, partial agonist or antagonist, and affinity, as described herein. After such testing, the CDLs can be further refined by generating LBD crystals with a CDL bound to the LBD. The structure of the CDL can then be further refined using the chemical modification methods described herein for three dimensional models to improve the activity or affinity of the CDL and make second generation CDLs with 25 improved properties, such as that of a super agonist or antagonist described herein. Agonist and antagonist ligands also can be selected that modulate nuclear receptor responsive gene transcription through altering the interaction of co-activators and corepressors with their cognate nuclear hormone receptor. For example, CDL agonists can be selected that block or dissociate the co-repressor from interaction with the 30 receptor, and/or which promote binding or association of the co-activator. CDL antagonists can be selected that block co-activator interaction and/or promote corepressor interaction with the target receptor. Selection can be done in binding assays that screen for CDLs having the desired agonist or antagonist properties. Suitable assays for such screening are described herein and in Shibata, H., et al. (Recent Prog.

Horm. Res. 52:141-164 (1997)); Tagami, T., et al. (Mol. Cell Biol. 17(5):2642-2648 (1997)); Zhu, XG., et al. (J. Biol. Chem. 272(14):9048-9054 (1997)); Lin, B.C., et al. (Mol. Cell Biol. 17(10):6131-6138 (1997)); Kakizawa, T., et al. (J. Biol. Chem. 272(38):23799-23804 (1997)); and Chang, K. H., et al. (Proc. Natl. Acad. Sci. USA 94(17):9040-9045 (1997)), which references are incorporated herein in their entirety by reference.

NUCLEAR RECEPTOR ISOFORMS

The present invention also is applicable to generating new synthetic ligands to distinguish nuclear receptor isoforms. As described herein, CDLs can be generated that distinguish between binding isoforms, thereby allowing the generation of either tissue specific or function specific synthetic ligands. For instance, GR subfamily members have usually one receptor encoded by a single gene, although are exceptions. For example, there are two PR isoforms, A and B, translated from the same mRNA by alternate initiation from different AUG codons. There are two GR forms, one of which does not bind ligand. This method is especially applicable to the TR subfamily which usually has several receptors that are encoded by at least two (TR: α, β) or three (RAR, RXR, and PPAR: α, β, γ) genes or have alternate RNA splicing and such an example for TR is described herein.

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NUCLEAR RECEPTOR CRYSTALS

The invention provides for crystals made from nuclear receptor ligand binding domains with the ligand bound to the receptor. As exemplified in the Examples, TRs are crystallized with a ligand bound to it. Crystals are made from purified nuclear receptor LBDs that are usually expressed by a cell culture, such as *E. coli*. Preferably, different crystals (co-crystals) for the same nuclear receptor are separately made using different ligands, such as a naturally occurring ligand and at least one bromo- or iodosubstituted synthetic ligand that acts as an analog or antagonist of the naturally occurring ligand. Such bromo- and iodo- substitutions act as heavy atom substitutions in nuclear receptor ligands and crystals of nuclear receptor proteins. This method has the advantage for phasing of the crystal in that it bypasses the need for obtaining traditional heavy metal derivatives. After the three dimensional structure is determined for the nuclear receptor LBD with its ligand bound, the three dimensional

structure can be used in computational methods to design a synthetic ligand for the nuclear receptor and further activity structure relationships can be determined through routine testing using the assays described herein and known in the art.

5 Expression and Purification of other Nuclear Receptor LBD Structures

High level expression of nuclear receptor LBDs can be obtained by the techniques described herein as well as others described in the literature. High level expression in E. coli of ligand binding domains of TR and other nuclear receptors, including members of the steroid/thyroid receptor superfamily, such as the receptors 10 ER, AR, MR, PR, RAR, RXR and VDR can also be achieved. Yeast and other eukaryotic expression systems can be used with nuclear receptors that bind heat shock proteins as these nuclear receptors are generally more difficult to express in bacteria, with the exception of ER, which can be expressed in bacteria. Representative nuclear receptors or their ligand binding domains have been cloned and sequenced: human 15 RAR-α, human RAR-γ, human RXR-α, human RXR-β, human PPAR-α, human PPAR-β, human PPAR-γ, human VDR, human ER (as described in Seielstad et al., Molecular Endocrinology, vol 9:647-658 (1995), incorporated herein by reference), human GR, human PR, human MR, and human AR. The ligand binding domain of each of these nuclear receptors has been identified and is shown in FIG. 3. Using the 20 information in FIG. 3 in conjunction with the methods described herein and known in the art, one of ordinary skill in the art could express and purify LBDs of any of the nuclear receptors, including those illustrated in FIG. 3, bind it to an appropriate ligand, and crystallize the nuclear receptor's LBD with a bound ligand.

FIG. 3 is an alignment of several members of the steroid/thyroid hormone
25 receptor superfamily that indicates the amino acids to be included in a suitable expression vector.

Extracts of expressing cells are a suitable source of receptor for purification and preparation of crystals of the chosen receptor. To obtain such expression, a vector is constructed in a manner similar to that employed for expression of the rat TR 30 alpha (Apriletti et al. Protein Expression and Purification, 6:363-370 (1995), herein incorporated by reference). The nucleotides encoding the amino acids encompassing the ligand binding domain of the receptor to be expressed, for example the estrogen receptor ligand binding domain (hER-LBD) (corresponding to R at position 725 to L

at position 1025 as standardly aligned as shown in the FIG. 3), are inserted into an expression vector such as the one employed by Apriletti et al (1995). For the purposes of obtaining material that will yield good crystals it is preferable to include at least the amino acids corresponding to human TR-β positions 725 to 1025. Stretches of adjacent amino acid sequences may be included if more structural information is desired. Thus, an expression vector for the human estrogen receptor can be made by inserting nucleotides encoding amino acids from position 700 to the c-terminus at position 1071. Such a vector gives high yield of receptor in E. coli that can bind hormone (Seielstad *et al. Molecular Endocrinology 9*:647-658 (1995)). However, the c-terminal region beyond position 1025 is subject to variable proteolysis and can advantageously be excluded from the construct, this technique of avoiding variable proteolysis can also be applied to other nuclear receptors.

TR-α And TR-β As Examples of Nuclear receptor LBD Structure and Function 15 TR Expression, Purification And Crystallization

As an example of nuclear receptor structure of the ligand binding domain the α- and β- isoforms of TR are crystallized from proteins expressed from expression constructs, preferably constructs that can be expressed in E. coli. Other expression systems, such as yeast or other eukaryotic expression systems can be used. For the TR, the LBD can be expressed without any portion of the DBD or amino-terminal domain. Portions of the DBD or amino-terminus can be included if further structural information with amino acids adjacent the LBD is desired. Generally, for the TR the LBD used for crystals will be less than 300 amino acids in length. Preferably, the TR LBD will be at least 150 amino acids in length, more preferably at least 200 amino acids in length, and most preferably at least 250 amino acids in length. For example the LBD used for crystallization can comprise amino acids spanning from Met 122 to Val 410 of the rat TR-α, Glu 202 to Asp 461 of the human TR-β.

Typically TR LBDs are purified to homogeneity for crystallization. Purity of TR LBDs is measured with sodium dodecyl sulfate polyacrylamide gel 30 electrophoresis (SDS-PAGE), mass spectrometry (MS) and hydrophobic high performance liquid chromatography (HPLC). The purified TR for crystallization should be at least 97.5 % pure or 97.5%, preferably at least 99.0% pure or 99.0% pure, more preferably at least 99.5% pure.

Initially purification of the unliganded receptor can be obtained by conventional techniques, such as hydrophobic interaction chromatography (HPLC), ion exchange chromatography (HPLC), and heparin affinity chromatography.

To achieve higher purification for improved crystals of nuclear receptors, 5 especially the TR subfamily and TR, it will be desirable to ligand shift purify the nuclear receptor using a column that separates the receptor according to charge, such as an ion exchange or hydrophobic interaction column, and then bind the eluted receptor with a ligand, especially an agonist. The ligand induces a change in the receptor's surface charge such that when re-chromatographed on the same column, 10 the receptor then elutes at the position of the liganded receptor are removed by the original column run with the unliganded receptor. Usually saturating concentrations of ligand are used in the column and the protein can be preincubated with the ligand prior to passing it over the column. The structural studies detailed herein indicate the general applicability of this technique for obtaining super-pure nuclear receptor LBDs for crystallization.

More recently developed methods involve engineering a "tag" such as with histidine placed on the end of the protein, such as on the amino terminus, and then using a nickle chelation column for purification, Janknecht R., *Proc. Natl. Acad. Sci. USA*, 88:8972-8976 (1991) incorporated by reference.

20 To determine the three dimensional structure of a TR LBD, or a LBD from another member of the nuclear receptor superfamily, it is desirable to co-crystalize the LBD with a corresponding LBD ligand. In the case of TR LBD, it is preferable to separately co-crystalize it with ligands such as T3, IpBr and Dimit that differ in the heavy atoms which they contain. Other TR ligands such as those encompassed by 25 Formula 1 described herein and known in the prior art, can also be used for the generation of co-crystals of TR LBD and TR ligands. Of the compounds encompassed by Formula 1 it is generally desirable to use at least one ligand that has at least one bromo- or iodo- substitution at the R₃, R₅, R₃' or R₅' position, preferably such compounds will be have at least two such substitutions and more preferably at 30 least 3 such substitutions. As described herein, such substitutions are advantageously used as heavy atoms to help solve the phase problem for the three dimensional structure of the TR LBD and can be used as a generalized method of phasing using a halogen (e.g. I or Br) substituted ligand, especially for nuclear receptors.

Typically purified LBD, such as TR LBD, is equilibrated at a saturating concentration of ligand at a temperature that preserves the integrity of the protein. Ligand equilibration can be established between 2 and 37°C, although the receptor tends to be more stable in the 2-20°C range.

Preferably crystals are made with the hanging drop methods detailed herein. Regulated temperature control is desirable to improve crystal stability and quality. Temperatures between 4 and 25°C are generally used and it is often preferable to test crystallization over a range of temperatures. In the case of TR it is preferable to use crystallization temperatures from 18 to 25°C, more preferably 20 to 23°C, and most 10 preferably 22°C.

Complexes of the TR- α LBD with a variety of agonists, including T₃, IpBr₂, Dimit, and Triac, are prepared with by methods described herein. For example, cocrystals of the rTR-a LBD, with ligand prebound, are prepared by vapor diffusion at ambient temperature from 15% 2-methyl-2,4-pentanediol (MPD). The crystals are 15 radiation sensitive, and require freezing to measure complete diffraction data. On a rotating anode X-ray source, the crystals diffract to ~3Å; synchrotron radiation extends the resolution limit significantly, to as high as 2.0Å for T₃ cocrystals. The composition of the thyroid hormone, combined with the ability to prepare and cocrystallize the receptor complexed with a variety of analogs, permitted the unusual 20 phasing strategy. This phasing strategy can be applied to the ligands of the nuclear receptors described therein by generating I and Br substitutions of such ligands. In this strategy, cocrystals of the TR LBD containing four hormone analogs that differ at the 3,5, and 3' positions (T3, IpBr2, Dimit, and Triac) provided isomorphous derivatives. For this set of analogs, the halogen substituents (2Br and 3I atoms) 25 function as heavy atoms, while the Dimit cocrystal (3 alkyl groups) acts as the parent. The initial 2.5Å multiple isomorphous replacement/anomalous scattering/density modified electron density map allowed the LBD to be traced from skeletons created in the molecular graphics program O5 (Jones, T.A. et al., ACTA Cryst, 47:110-119 (1991), incorporated by reference herein). A model of the LBD was built in four 30 fragments, Arg157-Gly184, Trp186-Gly197, Ser199-Pro205, and Val210-Phe405, and refined in XPLOR using positional refinement and simulated annealing protocols. Missing residues were built with the aid of difference density. The final model was refined to $R_{cryst} = 21.8\%$ and $R_{free} = 24.4\%$ for data from 15.0 to 2.2Å, see **Table 6**.

The human TR- β LBD model was resolved by molecular replacement of the TR- α LBD coordinates. The structure is based on E202 to D461 with a his-tag at the N-terminus. The final model was refined to $R_{cryst} = 25.3\%$ and $R_{free} = 28.9\%$ for data from 30.0 to 2.4Å+, see Table 7.

This phasing strategy can be applied to the ligands of the nuclear receptors described herein by generating I and Br substitutions of such ligands.

THREE DIMENSIONAL STRUCTURE OF TR LBD Architecture of TR LBD

As an example of the three dimensional structure of a nuclear receptor, the folding of the TR-α LBD is shown in FIG. 4. The TR-α LBD consists of a single structural domain packed in three layers, composed of twelve α-helices, H1-12, and four short β-strands, S1-4, forming a mixed β-sheet. The buried hormone and three antiparallel α-helices, H5-6, H9, and H10, form the central layer of the domain, as shown in FIG. 4. H1, H2, H3 and S1 form one face of the LBD, with the opposite face formed by H7, H8, H11, and H12. The first 35 amino acids of the N-terminus (Met122-Gln156) are not visible in the electron density maps. The three dimensional structure of the heterodimeric RXR:TR DNA-binding domains bound to DNA, amino acids Met 122 - Gln151 of the TR DBD make extensive contacts with the minor 20 groove of the DNA8. The five disordered amino acids (Arg152-Gln156), which reside between the last visible residue of the TR DBD and the first visible residue of the LBD likely represent the effective "hinge" linking the LBD and the DBD in the intact receptor.

The predominantly helical composition and the layered arrangement of 25 secondary structure is identical to that of the unliganded hRXRα, confirming the existence of a common nuclear receptor fold between two nuclear receptors.

The TR LBD is visible beginning at Arg157, and continues in an extended coil conformation to the start of H1. A turn of α-helix, H2, covers the hormone binding cavity, immediately followed by short β-strand, S1, which forms the edge of the 30 mixed β-sheet, parallel to S4, the outermost of the three antiparallel strands. The chain is mostly irregular until H3 begins, antiparallel to H1. H3 bends at Ile221 and Ile222, residues which contact the ligand. The chain turns almost 90° at the end of H3 to form an incomplete α-helix, H4. The first buried core helix, H5-6, follows, its axis

altered by a kink near the ligand at Gly 253. The helix is composed of mostly hydrophobic sidechains interrupted by two striking exceptions: Arg262 is solvent inaccessible and interacts with the ligand carboxylate (1-substituent), and Glu256 meets Arg329 from H9 and Arg375 from H11 in a polar invagination. H5-6 5 terminates in a short β-strand, S2, of the four strand mixed sheet. S3 and S4 are joined through a left-handed turn, and further linked by a salt bridge between Lys284 and Asp272. Following S4, H7 and H8 form an L, stabilized by a salt bridge between Lys268 and Asp277. The turn between H7 and H8 adopts an unusual conformation, a result of interaction with ligand and its glycine rich sequence. H9 is the second core 10 helix, antiparallel to the neighboring H5-6. Again, two buried polar sidechains are found, Glu315 and Gln320. Glu315 forms a buried salt bridge with His358 and Arg356. The oxygen of Gln320 forms a hydrogen bond with the buried sidechain of His 175. The chain then switches back again to form H10, also antiparallel to H9. H11 extends diagonally across the full length of the molecule. Immediately after H11, the 15 chain forms a type II turn, at approximately 90° to H11. The chain then turns again to form H 12, which packs loosely against H3 and H11 as part of the hormone or ligand binding cavity. The final five amino acids at the C-terminus, Glu406 -Val410, are disordered. The architecture of the TR- β LBD is identical to that of the TR- α LBD, with two significant differences. An additional helix is present at the N-terminus 20 (residues Glu202-I1e208), which is part of the DBD, and packs antiparallel to H10. Following the helix is a two residue turn (Gly209-His210) continuing into an extended coil to he start of H1, as seen in the TR-α LBD. A further difference occurs in the irregular conformation adopted between H2 and H3. In the TR-α LBD, residue Gly197-Asp211 form a loop that packs against the receptor, contacting helices H7, 25 H8, H11, and the loop between H11 and H12. In the TR-β LBD, only the ends of the loop are ordered, with the stretch Ala253-Lys263 disordered. In addition to these residues, the residues of the His-tag at the N-terminus, and the final residue at the Cterminus, Asp461, are disordered.

30 TR LBD's Ligand Binding Cavity As An Example Of A Nuclear Receptor's Buried Ligand Cavity

The three dimensional structure of the TR LBD leads to the startling finding that ligand binding cavity of the LBD is solvent inaccessible when a T3 or its isostere

is bound to the LBD. This surprising result leads to a new model of nuclear receptor three dimensional structure and function, as further described herein, particularly in the sections elucidating the computational methods of ligand design and the application of such methods to designing nuclear receptor synthetic ligands that 5 contain extended positions that prevent normal activation of the activation domain.

Dimit, the ligand bound to the receptor, is an isostere of T₃ and a thyroid hormone agonist. Therefore the binding of Dimit should reflect that of T₃, and the Dimit-bound receptor is expected to be the active conformation of TR. The ligand is buried within the receptor, providing the hydrophobic core for a subdomain of the 10 protein, as shown in FIG. 5 a and b. H5-6 and H9 comprise the hydrophobic core for the rest of the receptor.

An extensive binding cavity is constructed from several structural elements. The cavity is enclosed from above by H5-6 (Met 256- Arg266), from below by H7 and H8 and the intervening loop (Leu287- Ile299), and along the sides by H2 (185- 187), by the turn between S3 and S4 (Leu276-Ser277), by H3 (Phe215-Arg228), by H11 (His381-Met388) and by H12 (Phe401-Phe405). The volume of the cavity defined by these elements, calculated by GRASP (Columbia University, USA) (600 Å3), is essentially the volume of the hormone (530 Å). The change in volume can be exploited for ligand design as described herein. The remaining volume is occupied by water molecules surrounding the amino-propionic acid substituent. FIG. 6 depicts various contacts (or interactions) between TR's LBD and the ligand.

The planes of the inner and outer (prime ring) rings of the ligand are rotated from planarity about 60° with respect to each other, adopting the 3'-distal conformation (in which the 3' substituent of the outer ring projects down and away 25 from the inner ring). The amino-propionic acid and the outer phenolic ring assume the transoid conformation, each on opposite sides of the inner ring. The torsion angle χ₁ for the amino-propionic acid is 300°.

The amino-propionic acid substituent is packed loosely in a polar pocket formed by side chains from H2, H4 and S3. The carboxylate group forms direct 30 hydrogen bonds with the guanidium group of Arg228 and the amino N of Ser277. In addition, Arg262, Arg266 and Asn179 interact with the carboxylate through water-mediated hydrogen bonds. The three arginine residues create a significantly positive local electrostatic potential, which may stabilize the negative charge of the

carboxylate. No hydrogen bond is formed by the amino nitrogen. The interactions of the amino-propionic acid substituent are consistent with the fact that Triac, which lacks the amino nitrogen, has a binding affinity equal to that of T₃, indicating that the amino nitrogen and longer aliphatic chain of T₃ do not contribute greatly to binding affinity.

The biphenyl ether, in contrast, is found buried within the hydrophobic core. The inner ring packs in a hydrophobic pocket formed by H3, H5-6, and S3. Pockets for the 3- and 5-methyl substituents are not completely filled, as expected since the van der waals radius of methyl substituent for Dimit is smaller than the iodine substituent provided by the thyroid hormone T₃. Such pockets are typically 25 to 100 cubic angstroms (although smaller pocket for substitutes are contemplated in the 40 to 80 cubic angstrom range) and could be filled more tightly with better fitting chemical substitutions, as described herein.

The outer ring packed tightly in a pocket formed by H3, H5-6, H7, H8, H11

15 and H12, and the loop between H7 and H8. The ether oxygen is found in a hydrophobic environment defined by Phe218, Leu287, Leu276, and Leu292. The absence of a hydrogen bond to the ether oxygen is consistent with its role in establishing the correct stereochemistry of the phenyl rings, as suggested by potent binding of hormone analogs with structurally similar linkages possessing reduced or 20 negligible hydrogen bonding capability. The 3'-isopropyl substituent contacts Gly290 and 291. The presence of glycine at this position in the pocket can explain the observed relationship between activity and the size of 3'-substituents. Activity is highest for 3'-isopropyl, and decreases with added bulk. The only hydrogen bond in the hydrophobic cavity is formed between the phenolic hydroxyl and His381 Ne2.

25 The conformation of His381 is stabilized by packing contacts provided by Phe405, and Met256.

The presence of a 5' substituent larger than hydrogen affects the binding affinity for hormone. The more abundant thyroid hormone, 3,5,3',5'-tetraiodo-L-thyronine (T₄), contains an iodine at this position, and binds the receptor with 2% of 30 the affinity of T₃. The structure suggests that discrimination against T₄ is accomplished through the combination of steric conflict by Met256 and possibly the constraints imposed by the geometry of the hydrogen bond from His381 to the phenolic hydroxyl. The 5' position is a preferred location for introducing a chemical

modification of C-H at the 5' of T3 or and TR agonist, as described herein, that produces an extension from the prime ring and results in the creation of an antagonist or partial agonist.

Deletion and antibody competition studies suggest the involvement of residues
5 Pro162 to Val202 in ligand binding. The region does not directly contact hormone in
the bound structure, although H2 packs against residues forming the polar pocket that
interacts with the amino-propionic acid group. One role for H2, then, is to stabilize
these residues in the bound state, H2, with β-strands S3 and S4, might also represent a
prevalent entry point for ligand, since the amino-propionic acid of the ligand is
10 oriented toward this region. Studies of receptor binding to T3 affinity matrices
demonstrate that only a linkage to the amino-propionic acid is tolerated, suggesting
that steric hindrance present in other linkages prevent binding. Furthermore, the
crystallographic temperature factors suggest the coil and β-strand region is most
flexible part of the domain FIG. 7. Participation of this region, part of the hinge
15 domain between the DBD and LBD, in binding hormone may provide structural
means for ligand binding to influence DNA binding, since parts of the Hinge domain
contact DNA.

TR LBD Transcriptional Activation Helix As An Example Of A Nuclear Receptor 20 Activation Domain

In addition to the startling finding that the ligand binding cavity is solvent inaccessible when loaded with a ligand, the activation helix of TR LBD presents a surface to the ligand cavity for interaction between at least one amino acid and the bound ligand. The C-terminal 17 amino acids of the TR, referred to as the activation helix or AF-2 (an example of an LBD activation domain), are implicated in mediating hormone-dependent transcriptional activation. Although, mutations of key residues within the domain decrease ligand-dependent activation it was unclear until the present invention whether such mutations directly affected ligand coordination. Although some mutations of this domain have been noted to reduce or abolish ligand binding, other mutations in more distant sites of the LBD have a similar effect.

Activation domains among nuclear receptors display an analogous three dimensional relationship to the binding cavity, which is a region of the LBD that binds the molecular recognition domain of a ligand, i.e. the activation domain

presents a portion of itself to the binding cavity (but necessarily the molecular recognition domain of the ligand). Many nuclear receptors are expected to have such domains, including the retinoid receptors, RAR and RXR, the glucocorticoid receptor GR, and the estrogen receptor ER. Based upon the TR's sequence, the domain is proposed to adopt an amphipathic helical structure. β-sheet or mixed secondary structures, could be present as activation domains in less related nuclear receptors.

Within the activation domain, the highly conserved motif ΦΦΧΕΦΦ, where Φ represents a hydrophobic residue, is proposed to mediate interactions between the receptors and transcriptional coactivators. Several proteins have been identified 10 which bind the TR in a hormone-dependent fashion. One of these, Trip1, is related to a putative yeast coactivator Sug1, and also interacts with both the C-terminal activation domain and a subset of the basal transcriptional machinery, suggesting a role in transactivation by the TR. Other proteins, such as RIP140, SRC1, (Onate, S.A. et. al., Science 270:1354-1357 (1995)) and TF-1 (see also Ledouarim, B., et. al., 15 EMBO J. 14:2020-2033 (1995)), and GRIP-1 (Heery, E., et al., Nature 387:733-736 (1997)) also interact with other nuclear receptors in a ligand dependent manner through the C-terminal domain. Binding of these proteins can be modulated using the TR ligands described herein especially those TR ligands with extensions that sterically hinder the interaction between the highly conserved motif and other 20 proteins.

The C-terminal activation domain of the TR forms an amphipathic helix, H12, which nestles loosely against the receptor to form part of the hormone binding cavity. The helix packs with the hydrophobic residues facing inward towards the hormone binding cavity, and the charged residues, including the highly-conserved glutamate, extending into the solvent, as shown in FIG. 8. The activation helix of TR LBD presents Phe 401 to the ligand binding cavity and permits direct coordination with the hormone i.e. such amino acids interact with the ligand forming a van der waals contact with the plane of the outer phenyl ring. Phe 405 also interacts with His 381, perhaps stabilizing its hydrogen bonding conformation, i.e. a favorable hydrogen bond interaction. Participation of Phe 401 and Phe 405 in binding hormone explains how mutation of these residues decreases hormone binding affinity. Furthermore, the impact of these mutations on activation likely derives from a role in stabilizing the domain in the bound structure through increased hydrogen bond interaction of dipole

interactions. Glu 403 extends into the solvent, emphasizing its critical role in transactivation. In its observed conformation, presented on the surface as an ordered residue, against a background of predominantly hydrophobic surface. Glu 403 is available to interact with activator proteins described herein, as shown in **FIG. 9**. The other charged residues, Glu 405 and Asp 406 are disordered, as the helix frays at Phe 405.

Two other sequences in the TR, τ2 and τ3, activate transcription when expressed as fusion proteins with a DNA-binding domain. The sequences, discovered in the TRB, correspond to TR-α residues Pro158-Ile168 in H1 (τ2), and Gly290-Leu3 10 19 in H8 and H9 (τ3). Unlike the C-terminal activation domain, τ2 and τ3 do not appear to represent modular structural units in the rat TR-I LBD, nor present a surface for protein-protein interactions: the critical aspartate/glutamate residues of τ3 are located on two separate helices, and do not form a single surface; the charged residues of τ2 are engaged in ion pair interactions with residues of the LBD. Thus, τ2 and τ3 may not function as activation domains in the context of the entire receptor.

Computational Methods For Designing A Nuclear Receptor LBD LIGAND

The elucidation of the three dimensional structure of a nuclear receptor ligand binding domain provides an important and useful approach for designing ligands to nuclear receptors using the computational methods described herein. By inspecting the FIGURES it can be determined that the nuclear receptor ligand is bound in a water inaccessible binding cavity in the LBD and that chemical moieties can be added to selected positions on the ligand. Such chemical modifications, usually extensions, can fill up the binding cavity represented in the FIGURES for a tighter fit (or less water) or can be used to disrupt or make contacts with amino acids not in contact with the ligand before the chemical modification was introduced or represented in a figure of the three dimensional model of the LBD. Ligands that interact with nuclear superfamily members can act as agonists, antagonists and partial agonists based on what ligand-induced conformational changes take place.

Agonists induce changes in receptors that place them in an active conformation that allows them to influence transcription, either positively or negatively. There may be several different ligand-induced changes in the receptor's conformation.

Antagonists, bind to receptors, but fail to induce conformational changes that alter the receptor's transcriptional regulatory properties or physiologically relevant conformations. Binding of an antagonist can also block the binding and therefore the actions of an agonist.

Partial agonists bind to receptors and induce only part of the changes in the receptors that are induced by agonists. The differences can be qualitative or quantitative. Thus, a partial agonist may induce some of the conformation changes induced by agonists, but not others, or it may only induce certain changes to a limited extent.

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Ligand-induced Conformational Changes

As described herein, the unliganded receptor is in a configuration that is either inactive, has some activity or has repressor activity. Binding of agonist ligands induces conformational changes in the receptor such that the receptor becomes more active, either to stimulate or repress the expression of genes. The receptors may also have non-genomic actions. Some of the known types of changes and/or the sequelae of these are listed herein.

Heat Shock Protein Binding

For many of the nuclear receptors ligand binding induces a dissociation of heat shock proteins such that the receptors can form dimers in most cases, after which the receptors bind to DNA and regulate transcription.

Nuclear receptors usually have heat shock protein binding domains that present a region for binding to the LBD and can be modulated by the binding of a 25 ligand to the LBD. Consequently, an extended chemical moiety (or more) from the ligand that stabilizes the binding or contact of the heat shock protein binding domain with the LBD can be designed using the computational methods described herein to produce a partial agonist or antagonist. Typically such extended chemical moieties will extend past and away from the molecular recognition domain on the ligand and 30 usually past the buried binding cavity of the ligand.

Dimerization and Heterodimerization

With the receptors that are associated with the hsp in the absence of the ligand, dissociation of the hsp results in dimerization of the receptors. Dimerization is due to

receptor domains in both the DBD and the LBD. Although the main stimulus for dimerization is dissociation of the hsp, the ligand-induced conformational changes in the receptors may have an additional facilitative influence. With the receptors that are not associated with hsp in the absence of the ligand, particularly with the TR, ligand 5 binding can affect the pattern of dimerization/heterodimerization. The influence depends on the DNA binding site context, and may also depend on the promoter context with respect to other proteins that may interact with the receptors. A common pattern is to discourage monomer formation, with a resulting preference for heterodimer formation over dimer formation on DNA.

Nuclear receptor LBDs usually have dimerization domains that present a region for binding to another nuclear receptor and can be modulated by the binding of a ligand to the LBD. Consequently, an extended chemical moiety (or more) from the ligand that disrupts the binding or contact of the dimerization domain can be designed using the computational methods described herein to produce a partial agonist or antagonist. Typically such extended chemical moieties will extend past and away from the molecular recognition domain on the ligand and usually past the buried binding cavity of the ligand.

DNA Binding

In nuclear receptors that bind to hsp, the ligand-induced dissociation of hsp 20 with consequent dimer formation allows, and therefore, promotes DNA binding. With receptors that are not associated (as in the absence of ligand), ligand binding tends to stimulate DNA binding of heterodimers and dimers, and to discourage monomer binding to DNA. However, ligand binding to TR, for example, tends to 25 decrease dimer binding on certain DNA elements and has minimal to no effect on increasing heterodimer binding. With DNA containing only a single half site, the ligand tends to stimulate the receptor's binding to DNA. The effects are modest and depend on the nature of the DNA site and probably on the presence of other proteins that may interact with the receptors. Nuclear receptors usually have DBDs that 30 present a region for binding to DNA and this binding can be modulated by the binding of a ligand to the LBD. Consequently, an extended chemical moiety (or more) from the ligand that disrupts the binding or contact of the DBD can be designed using the computational methods described herein to produce a partial agonist or antagonist. Typically such extended chemical moieties will extend past and away from the

molecular recognition domain on the ligand and usually past the buried binding cavity of the ligand.

Repressor Binding

Receptors that are not associated with hsp in the absence of ligand frequently act as transcriptional repressors in the absence of the ligand. This appears to be due, in part, to transcriptional repressor proteins that bind to the LBD of the receptors. Agonist binding induces a dissociation of these proteins from the receptors. This relieves the inhibition of transcription and allows the transcriptional transactivation functions of the receptors to become manifest.

Transcriptional Transactivation Functions

Ligand binding induces transcriptional activation functions in two basic ways.

The first is through dissociation of the hsp from receptors. This dissociation, with

consequent dimerization of the receptors and their binding to DNA or other proteins in the nuclear chromatin allows transcriptional regulatory properties of the receptors to be manifest. This may be especially true of such functions on the amino terminus of the receptors.

The second way is to alter the receptor to interact with other proteins involved 20 in transcription. These could be proteins that interact directly or indirectly with elements of the proximal promoter or proteins of the proximal promoter. Alternatively, the interactions could be through other transcription factors that themselves interact directly or indirectly with proteins of the proximal promoter. Several different proteins have been described that bind to the receptors in a ligand-25 dependent manner. In addition, it is possible that in some cases, the ligand-induced conformational changes do not affect the binding of other proteins to the receptor, but do affect their abilities to regulate transcription.

Nuclear receptors or nuclear receptor LBDs usually have activation domains modulated in part by a co-activator/co-repressor system that coordinately functions to 30 present a region for binding to DNA, and can be modulated by the binding of a ligand to the LBD. Consequently, an extended chemical moiety (or more) from the ligand that disrupts the binding or contact of the activation domain with co-activator and/or co-repressor can be designed using the computational methods described herein to produce a partial agonist or antagonist. For instance, an agonist can be designed

and/or selected which (1) blocks binding and/or dissociates co-repressor, and/or (2) promotes binding and/or association of a co-activator. An antagonist can be designed which (1) promotes binding and/or association of co-repressor, and/or (2) promotes binding and/or association of co-activator. Ratios of agonists and antagonists may be 5 used to modulate transcription of the gene of interest. Selection can be accomplised in binding assays that screen for ligands having the desired agonist or antagonist properties, including such ligands which induce conformational changes as decribed below. Suitable assays for such screening are described herein and in Shibata, H., et al. (Recent Prog. Horm. Res. 52:141-164 (1997)); Tagami, T., et al. (Mol. Cell Biol. 10 17(5):2642-2648 (1997)); Zhu, XG., et al. (J. Biol. Chem. 272(14):9048-9054 (1997)); Lin, B.C., et al. (Mol. Cell Biol. 17(10):6131-6138 (1997)); Kakizawa, T., et al. (J. Biol. Chem. 272(38):23799-23804 (1997)); and Chang, K. H., et al. (Proc. Natl. Acad. Sci. USA 94(17):9040-9045 (1997)). Typically such extended chemical moieties will extend past and away from the molecular recognition domain on the 15 ligand and usually past the buried binding cavity of the ligand and in the direction of the activation domain, which is often a helix as seen in the three dimensional model shown in the FIGURES in two dimensions on paper or more conveniently on a computer screen.

20 Ligand-Induced Conformational Change

Plasma proteins bind hormones without undergoing a conformational change through a static binding pocket formed between monomers or domains. For example, the tetrameric thyroid-binding plasma protein transthyretin forms a solvent-accessible hormone-binding channel at the oligomer interface. The structure of the protein is unchanged upon binding hormone with respect to the appearance of a buried binding cavity with a ligand bound.

However, the structural role for a ligand bound to a nuclear receptor LBD, like rat TR-α LBD, predicts that the receptor would differ in the bound and unbound states. In the absence of hormone, the receptor would possess a cavity at its core, 30 uncharacteristic of a globular protein. A ligand (e.g. hormone) completes the hydrophobic core of the active receptor after it binds to the nuclear receptor. Ligand binding by the receptor is a dynamic process, which regulates receptor function by inducing an altered conformation.

An exact description of the hormone-induced conformational changes requires comparison of the structures of the liganded and the unliganded TR. The structure of the unliganded human RXRα may substitute as a model for the unliganded TR. The rat TR-α LBD and human RXRα LBDs adopt a similar fold, and it is likely that the structural similarity extends to the conformational changes after ligand binding.

There are three major differences between the two structures, which indeed appear to be the result of ligand binding. First, the bound rat TR-α LBD structure is more compact, with the hormone tightly packed within the hydrophobic core of the receptor. By contrast, the unliganded human RXRα LBD contains several internal 10 hydrophobic cavities. The presence of such cavities is unusual in folded proteins, and is likely a reflection of the unliganded state of the receptor. Two of these cavities were proposed as possible binding sites for 9-cis retinoic acid, though these multiple sites only partly overlap with the single buried binding cavity observed in the liganded rat TR-α LBD.

The second difference involves H11 in the rat TR-α LBD, which contributes part of the hormone binding cavity. H11, continuous in the rat TR-α LBD, is broken at Cys 432 in the RXR, forming a loop between H10 and H11 in the hRXRα. This residue corresponds to His381 in the TR, which provides a hydrogen bond to the outer ring hydroxyl of the ligand. Furthermore, the hormone binding cavity occupied by ligand in the rat TR-α LBD is interrupted in the hRXRα by the same loop, forming an isolated hydrophobic pocket in the RXR with H6 and H7. In the bound rat TR-α LBD, the corresponding helices H7 and H8 are contiguous with the binding pocket, and enclose the hormone binding cavity from below.

The third difference between the two receptors is the position of the C25 terminal activation domain. While the C-terminal activation domain forms α-helices
in both receptors, the domain in the rat TR-α LBD follows a proline-rich turn, and lies
against the receptor to contribute part of the binding cavity. In contrast, the activation
domain in the unliganded hRXRα, is part of a longer helix which projects into the
solvent.

These differences lead to a model for an alternate conformation of the TR LBD assumed in the absence of ligand. In the unliganded TR, the subdomain of the receptor surrounding the hormone binding cavity is loosely packed, with the binding cavity occluded by a partly unstructured H11 providing a partial core for the receptor.

Upon binding hormone, residues which form a coil in the unbound receptor engage the ligand, and continues H11. The ordering of H11 could unblock the hydrophobic cavity, allowing H7 and H8 to interact with hormone. The extended hydrophobic cavity then collapses around the hormone, generating the compact bound 5 structure.

It is possible to predict ligand-induced conformational changes in the C-terminal activation domain that rely, in part, on an extended structure in the unliganded TR that repacks upon ligand binding. The ligand- induced conformation change can be subtle since the amino acid sequence of the rat TR-α in the turn (393-10 PTELFPP-399) significantly reduces the propensity of the peptide chain of the rat TR-α to form an α-helix and therefore repacking can be accomplished with a minor change in volume.

After the ligand-induced conformational change occurs, it is likely that the conformation of the C-terminal activation domain in the bound structure changes 15 packing compared to the unbound form of the receptor. Binding of the ligand improves the stability of the activation domain. The activation domain packs loosely even in the bound structure, as measured by the distribution of packing interactions for the entire LBD. The packing density for the activation domain, defined as the number of atoms within 4.5Å, is 1.5 standard deviations below the mean. For 20 comparison, another surface helix, H1, is 0.5 standard deviations below the mean and the most poorly packed part of the structure, the irregular coil from residues Ile196-Asp206, is 2.0 standard deviations below the mean. Moreover, the majority of packing contacts for the C-terminal domain in the bound receptor are provided either by residues which interact with ligand, such as His381, or by the ligand itself. The 25 conformation of these residues can be expected to be different in the bound and unbound receptors, and by extension the conformation of C-terminal activation domain which relies upon these interactions. Without the stabilization provided by a bound ligand, it is likely that the C-terminal activation domain is disordered prior to hormone binding.

The interrelation of ligand-induced conformational changes is evident as described herein. For example, His381 from H11 and Phe405 from H12 interact in the bound structure to provide a specific hydrogen bond to the phenolic hydroxyl. The

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ligand-induced changes which affect H11 and H12 are reinforcing, and lead to the formation of the compact, bound state.

Comparison of the TR- α and TR- β LBD structures shows similar packing of the helices when complexed with the ligand Triac.

COMPUTATIONAL METHODS USING THREE DIMENSIONAL MODELS AND EXTENSIONS OF LIGANDS

The three-dimensional structure of the liganded TR receptor is unprecedented, and will greatly aid in the development of new nuclear receptor synthetic ligands, 10 such as thyroid receptor antagonists and improved agonists, especially those that bind selectively to one of the two TR isoforms (α or β). In addition, this receptor superfamily is overall well suited to modern methods including three-dimensional structure elucidation and combinatorial chemistry such as those disclosed in EP 335 628, U.S. patent 5,463,564, which are incorporated herein by reference. Structure 15 determination using X-ray crystallography is possible because of the solubility properties of the receptors. Computer programs that use crystallography data when practicing the present invention will enable the rational design of ligand to these receptors. Programs such as RASMOL can be used with the atomic coordinates from crystals generated by practicing the invention or used to practice the invention by 20 generating three dimensional models and/or determining the structures involved in ligand binding. Computer programs such as INSIGHT and GRASP allow for further manipulation and the ability to introduce new structures. In addition, high throughput binding and bioactivity assays can be devised using purified recombinant protein and modern reporter gene transcription assays described herein and known in the art in 25 order to refine the activity of a CDL.

Generally the computational method of designing a nuclear receptor synthetic ligand comprises two steps:

- determining which amino acid or amino acids of a nuclear receptor LBD interacts with a first chemical moiety (at least one) of the ligand using a three
 dimensional model of a crystallized protein comprising a nuclear receptor LBD with a bound ligand, and
 - 2) selecting a chemical modification (at least one) of the first chemical moiety to produce a second chemical moiety with a structure to either decrease or increase an

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interaction between the interacting amino acid and the second chemical moiety compared to the interaction between the interacting amino acid and the first chemical moiety.

As shown herein, interacting amino acids form contacts with the ligand and 5 the center of the atoms of the interacting amino acids are usually 2 to 4 angstroms away from the center of the atoms of the ligand. Generally these distances are determined by computer as discussed herein and in McRee 1993, however distances can be determined manually once the three dimensional model is made. Examples of interacting amino acids are described in Appendix 2. See also Wagner et al., Nature 10 378(6558):670-697 (1995) for stereochemical figures of three dimensional models. More commonly, the atoms of the ligand and the atoms of interacting amino acids are 3 to 4 angstroms apart. The invention can be practiced by repeating steps 1 and 2 to refine the fit of the ligand to the LBD and to determine a better ligand, such as an agonist. As shown in the FIGURES the three dimensional model of TR can be 15 represented in two dimensions to determine which amino acids contact the ligand and to select a position on the ligand for chemical modification and changing the interaction with a particular amino acid compared to that before chemical modification. Structural comparison of LBD isoforms complexed with the same or similar ligand permit identification of fiducial and adjustable amino acids that can be 20 exploited in designing isoform-specific ligands through chemical modification. "Fiducial" refers to amino acids that form rigid features of the ligand binding cavity. "Adjustable" refers to amino acids that form less rigid features of the ligand binding cavity. The chemical modification may be made using a computer, manually using a two dimensional representation of the three dimensional model or by chemically 25 synthesizing the ligand. The three dimensional model may be made using Appendix 2 and the FIGURES. As an additional step, the three dimensional model may be made using atomic coordinates of nuclear receptor LBDs from crystallized protein as known in the art, see McRee 1993 referenced herein.

The ligand can also interact with distant amino acids after chemical modification of the ligand to create a new ligand. Distant amino acids are generally not in contact with the ligand before chemical modification. A chemical modification can change the structure of the ligand to make as new ligand that interacts with a distant amino acid usually at least 4.5 angstroms away from the ligand. Often distant

amino acids will not line the surface of the binding cavity for the ligand, as they are too far away from the ligand to be part of a pocket or surface of the binding cavity.

The interaction between an atom of a LBD amino acid and an atom of an LBD ligand can be made by any force or attraction described in nature. Usually the 5 interaction between the atom of the amino acid and the ligand will be the result of a hydrogen bonding interaction, charge interaction, hydrophobic interaction, van der waals interaction or dipole interaction. In the case of the hydrophobic interaction it is recognized that this is not a per se interaction between the amino acid and ligand, but rather the usual result, in part, of the repulsion of water or other hydrophilic group 10 from a hydrophobic surface. Reduction or enhancment of the interaction of the LBD and a ligand can be measured by standard binding procedures, calculating or testing binding energies, computationally or using thermodynamic or kinetic methods as known in the art.

Chemical modifications will often enhance or reduce interactions of an atom 15 of a LBD amino acid and an atom of an LBD ligand. Steric hinderance will be a common means of changing the interaction of the LBD binding cavity with the activation domain. Chemical modifications are preferably introduced at C-H, C- and C-OH position in ligands, where the carbon is part of the ligand structure which remains the same after modification is complete. In the case of C-H, C could have 1, 2 or 3 hydrogens, but usually only one hydrogen will be replaced. The H or OH are removed after modification is complete and replaced with the desired chemical moiety.

Because the thyroid receptor is a member of the larger superfamily of hormone-binding nuclear receptors, the rules for agonist and antagonist development will be recognized by one skilled in the art as useful in designing ligands to the entire superfamily. Examining the structures of known agonists and antagonists of the estrogen and androgen receptors supports the generality of antagonist mechanism of action as shown in **FIG. 10**.

The overall folding of the receptor based on a comparison of the reported structure of the unliganded RXR and with amino acid sequences of other superfamily members reveals that the overall folding of receptors of the superfamily is similar. Thus, it is predicted from the structure that there is a general pattern of folding of the nuclear receptor around the agonist or antagonist ligand.

The three dimensional structure of a nuclear receptor with a ligand bound leads to the nonobvious observation that a nuclear receptor folds around agonist ligands, as the binding cavity fits the agonist, especially the agonist's molecular recognition domain, and antagonists commonly have chemical structures that extend 5 beyond the ligand, especially the agonist, and would prohibit folding of the receptor around the ligand to form a buried binding cavity or other groups that have the same effect. The location of the extension could affect the folding in various ways as indicated by the structure. Such extensions on antagonists are shown in **FIG. 10** for various receptors and compared to the corresponding agonist.

10 For example, an extension towards the carboxy-terminal activation helix affects the packing/folding of this helix into the body of the receptor. This in turn can affect the ability of this portion of the nuclear receptor to interact with other proteins or other portions of the receptor, including transcriptional transactivation functions on the opposite end of the linear receptor, or the receptor's amino terminus that may 15 interact directly or indirectly with the carboxy-terminal transactivation domain (including helix 12). Extensions in this direction can also affect the packing of helix 11 of TR (or its analogous helix in nuclear receptors) into the body of the receptor and selectively affect dimerization and heterodimerization of receptors. An extension pointing towards helix 1 can affect the relationship of the DNA binding domain and 20 hinge regions of the receptors with the ligand binding domain and selectively or in addition affect the receptors' binding to DNA and/or interactions of receptors with proteins that interact with this region of the receptor. Other extensions towards helix 11 can be made to affect the packing of this helix and helices 1 and 10 and thereby homo- and hetero-dimerization. Such chemical modifications can be assessed using 25 the computational methods described herein. It is also possible that, in some cases, extensions may protrude through the receptor that is otherwise completely or incompletely folded around the ligand. Such protruding extensions could present a steric blockade to interactions with co-activators or other proteins.

The three dimensional structure with the ligand buried in the binding cavity immediately offers a simple description of a nuclear receptor that has a binding cavity that contains hinges and a lid, composed of one or more structural elements, that move to accommodate and surround the ligand. The ligand to TR can be modified on specific sites with specific classes of chemical groups that will serve to leave the lid and hinge region in open, partially open or closed states to achieve partial agonist or

antagonist functions. In these states, the biological response of the TR is different and so the structure can be used to design particular compounds with desired effects.

Knowledge of the three-dimensional structure of the TR-T₃ complex leads to a general model for agonist and antagonist design. An important novel feature of the structural data is the fact that the T₃ ligand is completely buried within the central hydrophobic core of the protein. Other ligand-receptor complexes belonging to the nuclear receptor superfamily will have a similarly buried ligand binding site and therefore this model will be useful for agonist/antagonist design for the entire superfamily.

When design of an antagonist is desired, one needs either to preserve the important binding contacts of natural hormone agonist while incorporating an "extension group" that interferes with the normal operation of the ligand-receptor complex or to generate the requisite binding affinity through the interactions of the extensions with receptor domains.

The model applied to antagonist design and described herein is called the 15 "Extension Model." Antagonist compounds for nuclear receptors should contain the same or similar groups that facilitate high-affinity binding to the receptor, and in addition, such compounds should contain a side chain which may be large and/or polar. This side chain could be an actual extension, giving it bulk, or it could be a 20 side group with a charge function that differs from the agonist ligand. For example, substitution of a CH3 for CH2OH at the 21-position, and alteration at the 11-position from an OH group to a keto group of cortisol generates glucocorticoid antagonist activity (Robsseau, G.G., et. al., J. Mol. Biol. 67:99-115 (1972)). However, in most cases effective antagonists have more bulky extensions. Thus, the antiglucocorticoid 25 (and antiprogestin) RU486 contains a bulky side group at the 11-position (Horwitz, K.B. Endocrine Rev. 13:146-163 (1992)). The antagonist compound will then bind within the buried ligand binding site of the receptor with reasonably high affinity (100 nM), but the extension function will prevent the receptor-ligand complex from adopting the necessary conformation needed for transcription factor function. The 30 antagonism (which could be in an agonist or antagonist) may manifest itself at the molecular level in a number of ways, including by preventing receptor homo/heterodimer formation at the HRE, by preventing coactivator binding to receptor monomers, homodimers or homo/heterodimers, or by a combination of these effects which otherwise prevent transcription of hormone responsive genes mediated

by ligand-induced effects on the HRE. There are several antagonist compounds for nuclear receptors in the prior art (see also Horwitz, K.B., Endocrine Rev. 13:146-163 (1992), Raunnaud J.P. et. al., J. Steroid Biochem. 25:811-833 (1986), Keiel S., et. al., Mol. Cell. Biol. 14:287-298 (1994) whose antagonist function can be explained by the extension hypothesis. These compounds are shown in FIG. 10 along with their agonist counterparts. Each of these antagonists contains a large extension group attached to an agonist or agonist analogue core structure. Importantly, these antagonist compounds were discovered by chance and not designed with a structure-function hypothesis such as the extension principle.

One method of design of a thyroid antagonist using the extension hypothesis is provided below as a teaching example. The three-dimensional structure of the TR-α Dimit complex combined with structure-activity data published in the prior art, especially those reference herein, can be used to establish the following ligand-receptor interactions which are most critical for high-affinity ligand binding.

15 A physical picture of these interactions is shown in **FIG. 6**. The figure describes the isolated essential contacts for ligand binding. Because the ligand is buried in the center of the receptor, the structural spacing between these isolated interactions is also important. Thus, our present knowledge of this system dictates that, for this example, a newly designed ligand for the receptor must contain a thyronine structural skeleton, or two substituted aryl groups joined by a one-atom spacer.

The general structure for an antagonist designed by the extension hypothesis is exemplified in the following general description of the substituents of a TR antagonist (referring to Formula 1): R₁ can have anionic groups such as a carboxylate, phosphonate, phosphate, sulfate or sulfite and is connected to the ring with a 0 to 3 atom linker, comprising one or more C, O, N, S atoms, and preferably a 2 carbon linker. Such R₁ can be optionally substituted with an amine (e.g. -NH₂). R₃ and R₅ are small hydrophobic groups such as -Br, -I, or -CH₃. R₃ and R₅ can be the same substituents or different. R₃' can be a hydrophobic group that may be larger than those of R₃ and R₅, such as -I, -CH₃, -isopropyl, -phenyl, -benzyl, 5 and 6 ring heterocycles. R₄' is a group that can participate in a hydrogen bond as either a donor or acceptor. Such groups include -OH, -NH₂, and -SH. R₅' is an important extension group that makes this compound an antagonist. R₅' can be a long chain alkyl (e.g. 1 to 9 carbons, straight chain or branched), aryl (benzyl, phenyl and substituted benzyl

and phenyl rings (e.g. with halogen, alkyl (1 and 5 carbons) and optionally connected to the ring by a -CH₂-), heterocycle (e.g. 5 or 6 atoms, preferably 5 carbons and 1 nitrogen, or five carbons), which can optionally include polar (e.g. -OH, -NH₂, and -SH), cationic (e.g. -NH₃, N(CH)₃), or anionic (carboxylate, phosphonate, phosphate or sulfate) groups. R₅' can also be a polar (e.g. -OH, -NH₂, and -SH), cationic (e.g. -NH₃, -N(CH₃)₃), and anionic (carboxylate, phosphonate, phosphate or sulfate) groups. X is the spacer group that appropriately positions the two aromatic rings. This group is usually a one-atom spacer, such as O, S, SO, SO₂, NH, NZ where Z is an alkyl, CH₂, CHOH, CO, C(CH₃)OH, and C(CH₃)(CH₃). X also may be NR₇, CHR₇, CR₇, Nere R₇, is an alkyl, aryl or 5- or 6-membered heterocyclic aromatic. R₂, R₆, R₂' and R₆' can be -F, and -Cl and are preferably H.

A TR ligand can also be described as a substituted phenylated 3,5 diiodo tyrosine with substituted R₅' and R₃' groups. R₅' can be a long chain alkyl (e.g. 4 to 9 carbons, straight chain or branched), aryl (benzyl, phenyl and substituted benzyl and 15 phenyl rings (e.g. with halogen, alkyl (1 and 5 carbons) and optionally connected to the ring by a -CH₂-), heterocycle (e.g. 5 or 6 atoms, preferably 5 carbons and 1 nitrogen, or five carbons), which can optionally include polar (e.g. -OH, -NH₂, and -SH), cationic (e.g. -NH₃, N(CH)₃), or anionic (carboxylate, phosphonate, phosphotae or sulfate) groups. R₅' can also be a polar (e.g. -OH, -NH₂, and -SH), cationic (e.g. - NH₃, N(CH)₃), and anionic (carboxylate, phosphonate, phosphate or sulfate) groups. R₃' can be -IsoPr, halogen, -CH₃, alkyl (1 to 6 carbons) or aryl (benzyl, phenyl and substituted benzyl and phenyl rings (e.g. with halogen, alkyl (1 and 5 carbons) and optionally connected to the ring by a -CH₂-), heterocycle (e.g. 5 or 6 atoms, preferably 5 carbons and 1 nitrogen, or five carbons), which can optionally include polar (e.g. - OH, -NH₂, and -SH), cationic (e.g. -NH₃, N(CH)₃), or anionic (carboxylate, phosphonate, phosphate or sulfate) groups.

A TR antagonist can also be a modified T₃ agonist (having a biphenyl structure) wherein R₅' is alkyl, aryl, 5- or 6-membered heterocyclic aromatic, heteroalkyl, heteroaryl, arylalkyl, heteroaryl alkyl, polyaromatic, polyheteroaromatic, polar or charged groups, wherein said R₅' may be substituted with polar or charged groups. The R₅' groups are defined, as described herein.

Using these methods the ligands of this example preferably have the following properties:

1. The compounds should bind to the TR with high affinity (for example 100 nM).

- 2. The compounds should bind the receptor in the same basic orientation as the natural hormone.
- 5 3. The extension group R₅' should project toward the activation helix (C-terminal helix) of the receptor.
 - 4. The appropriate substituent at R_5 ' should perturb the activation helix from its optimal local structure needed for mediating transcription.

Antagonists may also be designed with multiple extensions in order to block 10 more than one aspect of the folding at any time.

TR ligands (e.g. super agonists) can be designed (and synthesized) to enhance the interaction of at least one amino acid with at least one chemical moiety on the ligand's molecular recognition domain. One method is to enhance the charge and polar interactions by replacing the carboxylate of T₃ (R₁ position) with phosphonate, phosphate, sulfate or sulfite. This enhances the interaction with Arg 262, Arg 266 and Arg 228. The interaction of at least one amino acid with at least one chemical moiety on the ligand's molecular recognition domain can also be enhanced by increasing the size of R₁ group to fill the space occupied by water when Dimit is bound (referring to R₁). Preferably the group has a complementary charge and hydrophobicity to the binding cavity.

Another way of improving the interaction of at least one amino acid with at least one chemical moiety on the ligand's molecular recognition domain is to restrict the conformation of the dihedral angle between the two phenyl rings of the thyronine ligand in solution. In solution the planes of two phenyl rings are orthogonal where the dihedral angle is 90°. In the TR Dimit structure, the dihedral angle is close to 60°. A TR ligand design that fixes the angle between the two phenyl rings will lead to tighter binding. Such a ligand may be made by connecting the R₆' and the R₅ positions of a thyronine or a substituted thyronine-like biphenyl. The size of the cyclic connection can fix the angle between the two phenyl rings. Referring specifically to Formula 1, 30 the following cyclic modifications are preferred: 1) R₅ is connected to R₆', 2) R₃ is connected to R₂' or 3) R₅ is connected to R₆' and R₃ is connected to R₂'. The connections can be made by an alkyl or heteroalkyl chain having between 1 to 6 atoms and preferably from 2 to 4 carbon atoms or other atoms. Any position of the heteroalkyl chain can be N, O, P or S. The S and P heteroatoms along said heteroalkyl

chain are in any of their possible oxidative states. The N heteroatom or any carbon along the alkyl or heteroalkyl chain may have one or more Z substituents, wherein Z is alkyl, heteroalkyl, aryl, heteroaryl, 5- or 6-membered heterocyclic aromatic. These compounds can be claimed with the proviso that Formula 1 does not include any prior art compound as of the priority filing date of this application.

The interaction of at least one amino acid with at least one chemical moiety on the ligand's molecular recognition domain can also be enhanced by selecting a chemical modification that fills the unfilled space between a TR ligand and the LBD in the area of the bridging oxygen (such as in T3, Triac or Dimit). Thus, a slighter larger moiety that replaces the ether oxygen can enhance binding. Such a linker may be a mono- or geminal- disubstituted carbon group. A group approximately the same size as oxygen but with greater hydrophobicity is preferred as well as small, hydrophobic groups for the disubstituted carbon.

Compounds of Formula I or derivatives thereof that modulate TR activity also 15 may be designed and selected to interact with a conformationally constrained structural feature of a TR LBD that is conserved among TR LBD isoforms to increase TR-specific selectivity. Conserved structural features of a TR LBD include residues found in equivalent positions of TR LBD isoforms which interact with a conserved structural feature of a compound comprising the biphenyl scaffold (φ-X-φ) or a single 20 phenyl scaffold (φ-X or X-φ) of Formula I. Conformationally constrained structural features of a TR LBD include residues that have their natural flexible conformations fixed by various geometric and physical-chemical constraints, such as local backbone, local side chain, and topological constraints. These types of constraints are exploited to restrict positioning of atoms involved in receptor-ligand recognition and binding. 25 For example, comparison of atomic models of TR LBD isoforms bound to thyronine and thyronine-like ligands reveal that certain residues which contact the ligands are restricted to particular topological shapes and angles of rotation about bonds. These include Met259, Leu276, Leu292, His381, Gly290, Ile221, and Phe401 of TR-α. The corresponding positions in TR-β include Met313, Leu330, Leu346, His435, Glv344, 30 Ile275 and Phe455, respectively.

Selectivity imparted by conformationally constrained features of both the receptor and compound are of particular interest. For example, compounds of Formula I comprising constrained cyclic carbons and substituent groups that interact

with a constrained feature of a TR LBD can be exploited to further increase binding specificity while reducing the potential for cross-over interaction with other receptors. These include hydrophobic and/or hydrophilic contacts between constrained residues of a TR LBD and atomic groups of the following constituents of the compound in reference to Formula I: (i) the biphenyl rings; (ii) the R₃-substituent; (iii) the R₃'-substituent; and (iv) the R₄'-substituent.

For example, contacts to the phenyl moiety comprising the R₁, R₂, R₃, R₅ and R₆ substituents, i.e., the ring proximal to the polar pocket (the "inner ring"), include a cycle carbon atom that interacts with an atom of a hydrophobic residue of a TR LBD, such as a carbon and oxygen atom of Met259 and a carbon atom of Leu276 of TR-α, or Met313 and Leu330 of TR-β, where the cycle carbon is about 3.0 to 4.0A from the atom of the hydrophobic group. For example, comparison of TR-α complexed with T3 and TR-β complexed with GC-1 reveals the following conserved inner ring contacts:

15						
	<u>Ligand</u>	TR LB	TR LBD_			
	T3/Atom	TR-α Residue	Atom	Distance		
	C11	Met259	C	3.95		
	C11	Met259	O	3.59		
20	C11	Met259	CB	3.77		
	C7	Leu276	CD2	3.80		
	C9	Leu276	CD2	3.70		
	00111	mp		~ .		
	GC1/Atom	TR-β Residue	Atom	Distance		
25	C11	Met313	C	3.85		
	C11	Met313	O	3.41		
	C11	Met313	CB	3.79		
	C7	Leu330	CD2	3.56		
	C9	Leu330	CD2	3.63		
30						

Contacts to the phenyl moiety comprising the R₂', R₃', R₄', R₅' and R₆' substituents, i.e., the ring distal to the polar pocket (the "outer ring"), include a cyclic carbon atom that interacts with an atom of a hydrophobic residue of a TR LBD, such as a carbon atom of Leu292 of TR-α, or Leu346 of TR-β, where the cyclic carbon atom is about 3.0 to 4.0A from the atom of the hydrophobic residue. For example, comparison of TR-α complexed with T3 and TR-β complexed with GC-1 reveals the following conserved outer ring contacts:

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	<u>Ligand</u>	TR LB	TR LBD		
	T3/Atom	TR-α Residue	Atom	Distance	
	C6	Leu292	CD2	3.58	
	C8	Leu292	CD2	3.50	
5	GC1/Atom	TR-β Residue	Atom	Distance	
	C6	Leu346	CD2	3.77	
	C8	Leu346	CD2	3.80	

Contacts to the R₃-substituent include an atom that interacts with a carbon atom of a hydrophobic residue of a TR LBD, such as Ile221 of TR-α, or Ile275 of TR-β, where the R₃-substituent atom is about 3.0 to 4.0A from the carbon atom of the hydrophobic residue. For example, comparison of TR-α complexed with T3 and TR-β complexed with GC-1 reveals the following conserved R₃-substituent contacts:

15

	Ligand	TR LB		
	T3/Atom	TR-α Residue Ile221	Atom CG1	Distance 4.01
20	GC1/Atom C19	TR-β Residue Ile275	Atom CG1	Distance 3.98

Contacts to the R₃'-substituent include an atom that interacts with an atom of a hydrophobic or hydrophilic residue of a TR LBD, such as an oxygen atom of Gly290 of TR-α, or Gly344 of TR-β, where the R₃'-substituent atom is about 3.0 to 4.0A from the atom of the hydrophobic or hydrophilic residue. For example, comparison of TR-α complexed with T3 and TR-β complexed with GC-1 reveals the following conserved R₄'-substituent, phenolic hydroxyl contacts:

30	<u>Ligand</u>	TR LBD	
	T3/Atom I2	TR-α Residue Aton Gly290 O	n Distance 3.50
	GC1/Atom C18	TR-β Residue Aton Gly344 O	Distance 3.60

35

Contacts to the R₄'-substituent comprising a phenolic hydroxyl include carbon and oxygen atoms that interact with a hydrophobic or hydrophilic residue of a TR LBD, such as a carbon and nitrogen atom of His381 of TR-α, or His435 of TR-β,

where the R₄'-substituent atom is about 2.0 to 4.0A from an atom of the hydrophobic or hydrophilic residue. For example, comparison of TR-α complexed with T3 and TR-β complexed with GC-1 reveals the following conserved R₄'-substituent, phenolic hydroxyl contacts:

5			
	Ligand	TR LBD	-
	T3/Atom	TR-a Residue Atom	Distance
	C10	His381 CD2 3.97	
	O1	His381 CD2 3.39	
10	O1	His381 CE1 3.82	•
	C8	His381 NE2 3.47	
	C10	His381 NE2 3.55	
	O1	His381 NE2 2.70	
	GC1/Atom	TR-β Residue Atom	Distance
15	C10	His435 CD2 3.89	
	O1	His435 CD2 3.64	
	O1	His435 CE1 3.79	
	C8	His435 NE2 3.44	
	C10	His435 NE2 3.33	
20	O1	His435 NE2 2.77	

Contacts to the R₄'-substituent also may include an atom that interacts with a carbon atom of a hydrophobic residue of a TR LBD, such as Phe401 of TR-α, or 25 Phe455 of TR-β, for defining agonist activity, i.e., proper presentation of helix-12 (H12) of the TR LBD following ligand binding. The R₄'-substituent atom is about 3.0 to 4.0Å from the carbon atom of the hydrophobic group. For example, comparison of TR-α complexed with T3 and TR-β complexed with GC-1 reveals the following conserved R₄'-substituent contacts:

30				
	<u>Ligand</u>	TR LB	-	
	T3/Atom	TR-α Residue	Atom	Distance
	O1 .	Phe401	CE1	3.52
	O1	Phe401	CZ	3.32
35	GC1/Atom	TR-β Residue	Atom	Distance
	O1	Phe455	CE1	3.40
	O1	Phe455	CZ	3.22

40 Comparison of atomic models of TR LBD isoforms complexed with the same and/or different ligands therefore facilitates the identification of new compounds that

fit spacially and preferentially into a TR LBD. Modeling, comparison of TR-ligand overlays, and comparison of TR LBD isoforms also permit identification of conformationally conserved structural features of TR LBD/ligand contacts. Exploiting conformational constraints of the LBD-ligand interaction identified by such methods therefore improves the design and identification of new compounds having increased selectivity for binding a particular type of nuclear receptor, such as TR.

TR- α and TR- β Selectivity for the Thyroid Hormone Receptor

Using the method described herein ligands can be designed that selectively bind to the alpha more than the beta TR or vice versa. The X-ray crystallographic structure of the rat TR-α LBD provides insight into design of such ligands.

The three dimensional structure reveals that the major difference between the TR-α and TR-β in the ligand binding cavity resides in amino acid Ser 277 (with the side group -CH₂OH) in the rat TR-α and whose corresponding residue is 331, asparagine (with the side group -CH₂CONH₂), in the human TR-β. The side chain in human TR-β is larger, charged and has a different hydrogen bonding potential, which would allow the synthesis of compounds that discriminate between this difference. The Ser277 (Asn331 in TR-β) forms part of the polar pocket of the TR LBD, 20 indicating that for TR-α versus TR-β discrimination, ligands can be designed to contain chemical modification of the R1-substitutent with reference to Formula I that exploit this difference.

For example, in the complex of TR-α with Triac, Ser277 does not participate in ligand binding. The absence of a role for Ser277 (Asn331 in beta) is consistent 25 with the equal affinity of Triac for the alpha and beta isoforms, and indirectly supports the contention that alpha/beta selectivity resides in the amino acid substitution Ser277 to Asn331 and its interaction with Arg228. The effect of the amino acid substitution is further evident when the interactions of Asn331 and Arg282 in the structures of the TR-β LBD complexed with GC-1 or Triac are 30 compared with those of Ser277 and Arg228 in the TR-α LBD. In the complex with GC-1, Asn331 forms a hydrogen bond to Arg282, which in turn forms a hydrogen bond with the carboxylate of GC-1, a pattern that resembles the interactions of Ser277 and Arg228 in the complexes of the TR-α LBD complexed with T₃ or Triac

However, in the complex of TR-β with Triac, Arg282 rotates away from Asn331 and the ligand, instead forming hydrogen bonds to residues Thr287 and Asp291 of H3. Therefore, differences exist between the two isoforms in the conformation of the polar pocket, depending on the nature of the ligand R₁-substitutent, indicating that certain substituents may interact preferentially with the conformation of a given isoform.

Comparing overlays of various ligands bound to the TR-α versus TR-β LBDs shows the positioning of the ligand to be very similar. Surprisingly, comparison of the volume and area for the TR- α and TR- β LBDs bound by the same or different ligands unexpectedly shows that the cubic space or volume available for 10 accommodating ligand binding by the TR- β LBD (645 ± 28.28 Å³) is larger and more flexable than that of the TR- α LBD (596.25 ± 7.97 Å³) (Table 1). The volume of the ligand binding cavity for TR-\alpha varies over a narrow range of about 8+, with a maximum difference of about 16+. In contrast, the volume of the ligand binding cavity for TR-B differs by nearly 40+ between the complexes with GC-1 and Triac. 15 There also is a difference in the volume of the ligand binding cavity when comparing the same ligand bound to TR- α and TR- β . For example, TR- α and TR- β complexed with Triac differ in LBD volume by about 36 Å³. Comparison of TR-α and TR-β bound to Dimit and GC-1, respectively, which ligands have similar volume/area and superpositioned architecture, show that the difference in LBD volume is about 75 Å³. 20 These differences are attributed primarily to variable movement and interaction of side chain groups with ligand substitutents of the phenyl moiety (φ) of the biphenyl scaffold (φ-X-φ) located proximal to the polar pocket, e.g., R₁-substituents in reference to Formula I. In contrast, the volume available in the hydrophobic pocket for both the $TR-\alpha$ and $TR-\beta$ LBDs is substantially the same. For example, binding of 25 Triac to the TR-β LBD displaces the side chain of Arg 282 providing approximately 60 Å³ in the polar pocket cavity, exposing the polar pocket to bulk solvent exchange. For GC-1 bound to the TR-\$\beta\$ LBD, approximately 14 \delta^3 is due to side chain motion of Met310, and approximately 44 Å³ is due to side chain motion of Arg320, the combination of which increases the size of the polar pocket in the TR-B LBD. This 30 extra pliability also may explain the absence of ordered water in the polar pocket of TR-B LBD bound to Triac or GC-1, which is in contrast to the ordered water found in the polar pocket of TR- α LBD bound to Dimit, IpBr2 or T3.

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Table 1*

	rΊ	R-α		
·	Dimit	Triac	IpBr2	<u>T3</u>
TR LBD (volÅ ³ /areaÅ ²)	590/456	589/440	601/474	605/472
Ligand (volÅ ³ /areaÅ ²)	303/314	333/326	326/330	355/346
Complementarity	0.65	0.68	0.66	0.71

hTR-β					
	GC-1	<u>Triac</u>			
TR LBD (volÅ ³ /areaÅ ²)	665/575	625/474			
Ligand (volÅ ³ /areaÅ ²)	294/310	333/326			
Complementarity	0.61	0.67			

*TR LBD volume and area are reported in Angstroms measured by GRASP. Complementarity is determined as defined in Lawrence *et al.*, *J. Mol. Biol. 234*:946-950 (1993).

Residue Ser277 in TR-α and the corresponding residue Asn331 of TR-β also contribute to the volumetric differences observed in the polar pockets of these two TR isoforms. And substitution of the Asn331 of hTR-β with serine has the affect of modifying ligand binding affinity of TR-β so that it resembles that of TR-α (See Example 5). Taken together, differences in hydrogen bonding of atoms of the side chain group of Ser277 in TR-α and Asp331 in TR-β extending from the equivalent backbone position in these TR LBDs and the more restricted polar pocket of the TR-α LBD further supports the concept of designing TR LBD isoform-specific ligands 15 having substitutents that fit spacially and preferentially into the polar pocket of either the TR-α or TR-β LBDs. Exploitation of this difference provides an additional means for computational design of isoform-specific TR agonists and antagonists.

In terms of ligand design, these differences mean that for β -selective ligands, some or all of the following differences should be exploited:

- 20 1. The presence of a larger side chain asparagine.
 - 2. The ability of the carbonyl group on the side chain to provide a strong hydrogen bond acceptor.
 - The ability of the amido group on the side chain to provide a two hydrogen bond donors.
- 4. Adjustment of polarity to reorganize the trapped water in the T3 pocket.
 - 5. Greater size and flexibility of the polar pocket.

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In terms of pharmaceutical design, these differences mean that for α -selective ligands, some or all of the following differences should be exploited:

- 1. The presence of a smaller side group.
- 2. The ability of the hydroxyl on the -CH₂OH side group carbonyl group on the side chain to provide a weak hydrogen donor.
- 3. Adjustment of polarity to reorganize the trapped water in the T3 pocket.
- 4. Smaller size and limited flexibility of the polar pocket.

In both cases these differences can be exploited in a number of ways. For example, they can also be used with a software set for construction of novel organic molecules such as LUDI from Biosym-MSI. An example of designing TR-β selective ligands is increasing the polarity of a ligand substituent located in the polar pocket of a TR LBD through addition of one or more ligand groups having a formal negative charge and/or negative dipole charge that interacts with a formal positive charge and/or positive dipole charge of a group in the polar pocket of the LBD. This exploits preferential interactions, such as with the additional positive charge contributed by Asn 331 in TR-β. Another example of a TR-β selective ligand is one that comprises one or more groups which fit spacially into the TR-β LBD polar pocket. This exploits spacial differences between TR LBD isoforms, such as the larger and more flexible 20 polar pocket of TR-β.

METHODS OF TREATMENT

The compounds of Formula 1 can be useful in medical treatments and exhibit biological activity which can be demonstrated in the following tests:

25 (i) the induction of mitochondrial α-glycerophosphate dehydrogenase (GPDH:EC 1.1.99.5). This assay is particularly useful since in certain species e.g. rats it is induced specifically by thyroid hormones and thyromimetics in a close-related manner in responsive tissues e.g. liver, kidney and the heart (Westerfield, W.W., Richert, D.A. and Ruegamer, W.R., *Endocrinology* (1965) 77:802). The assay 30 allows direct measurement in rates of a thyroid hormone-like effect of compounds and in particular allows measurement of the direct thyroid hormone-like effect on the heart. Other measurements included parameters such as heart rate and cardiac

enzymes including Ca⁺⁺ ATPase, Na⁺⁺/K⁺ ATPase, myosin isoforms and specific liver enzymes;

- (ii) the elevation of basal metabolic rate as measured by the increase in whole body oxygen consumption (see e.g., Barker *et al.*, *Ann. N. Y. Acad. Sci.*, (1960) 5 86:545-562);
 - (iii) the stimulation of the rate of beating of atria isolated from animals previously dosed with thyromimetrics (see e.g., Stephan et al., Biochem. Pharmacol. (1992) 13:1969-1974; Yokoyama et al., J. Med. Chem., (1995) 38:695-707);
- (iv) the change in total plasma cholesterol levels as determined using a 10 cholesterol oxidase kit (for example, the Merck CHOD iodine colorimetric kit. see also, Stephan et al. (1992));
- (v) the measurement of LDL (low density lipoprotein) and HDL (high density lipoprotein) cholesterol in lipoprotein fractions separated by ultracentrifugation; and p (vi) the change in total plasma triglyceride levels as 15 determined using enzymatic color tests, for example the Merck System GPO-PAP method.

The compounds of Formula 1 can be found to exhibit selective thyromimetic activity in these tests,

- (a) by increasing the metabolic rate of test animals, and raising hepatic 20 GPDH levels at doses which do not significantly modify cardiac GPDH levels.
 - (b) by lowering plasma cholesterol and triglyceride levels, and the ratio of LDL to HDL cholesterol at doses which do not significantly modify cardiac GPDH levels.

The compounds of Formula 1 may therefore be used in therapy, in the treatment of conditions which can be alleviated by compounds which selectively mimic the effects of thyroid hormones in certain tissues whilst having little or no direct thyromimetic effect on the heart. For example, compounds of Formula 1 which raise hepatic GPDH levels and metabolic rate at doses which do not significantly modify cardiac GPDH levels are indicated in the treatment of obesity.

Agonists of Formula 1 will lower total plasma cholesterol, the ratio of LDL-cholesterol to HDL-cholesterol and triglyceride levels at doses which do not significantly modify cardiac GPDH levels are indicated for use as general antihyperlipidaemic (antihyperlipoproteinaemic) agents i.e. in the treatment of patients having elevated plasma lipid (cholesterol and triglyceride) levels. In

addition, in view of this effect on plasma cholesterol and triglyceride, they are also indicated for use as specific anti-hypercholesterolemic and anti-hypertriglyceridaemic agents.

Patients having elevated plasma lipid levels are considered at risk of developing coronary heart disease or other manifestations of atherosclerosis as a result of their high plasma cholesterol and/or triglyceride concentrations. Further, since LDL-cholesterol is believed to be the lipoprotein which induces atherosclerosis, and HDL-cholesterol believed to transport cholesterol from blood vessel walls to the liver and to prevent the build up of atherosclerotic plaque, anti-hyperlipidemic agents which lower the ratio of LDL-cholesterol to HDL cholesterol are indicated as anti-atherosclerotic agents, herein incorporated by reference U.S. patents 4,826,876 and 5,466,861.

The present invention also provides a method of producing selective thyromimetic activity in certain tissues except the heart which comprises administering to an animal in need thereof an effective amount to produce said activity of a compound of Formula 1 or a pharmaceutically acceptable salt thereof.

The present invention also relates to a method of lowering plasma lipid levels and a method of lowering the ratio of LDL-cholesterol to HDL-cholesterol levels by suitably administering a compound of this invention or a pharmaceutically acceptable 20 sale thereof.

In addition, compounds of Formula 1 may be indicated in thyroid hormone replacement therapy in patients with compromised cardiac function.

In therapeutic use the compounds of the present invention are usually administered in a standard pharmaceutical composition.

The present invention therefore provides in a further aspect pharmaceutical compositions comprising a compound of Formula 1 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier. Such compositions include those suitable for oral, parenteral or rectal administration.

PHARMACEUTICAL COMPOSITIONS

Compounds of Formula 1 and their pharmaceutically acceptable salts which are active when given orally can be formulated as liquids for example syrups, 5 suspensions or emulsions, tablets, capsules and lozenges.

A liquid composition will generally consist of a suspension or solution of the compound or pharmaceutically acceptable salt in a suitable liquid carrier(s), for example ethanol, glycerine, sorbitol, non-aqueous solvent such as polyethylene glycol, oils or water, with a suspending agent, preservative, surfactant, wetting agent, flavoring or coloring agent. Alternatively, a liquid formulation can be prepared from a reconstitutable powder.

For example a powder containing active compound, suspending agent, sucrose and a sweetener can be reconstituted with water to form a suspension; and a syrup can be prepared from a powder containing active ingredient, sucrose and a sweetener.

A composition in the form of a tablet can be prepared using any suitable pharmaceutical carrier(s) routinely used for preparing solid compositions. Examples of such carriers include magnesium stearate, starch, lactose, sucrose, microcrystalline cellulose and binders, for example polyvinylpyrrolidone. The tablet can also be provided with a color film coating, or color included as part of the carrier(s). In addition, active compound can be formulated in a controlled release dosage form as a tablet comprising a hydrophilic or hydrophobic matrix.

A composition in the form of a capsule can be prepared using routine encapsulation procedures, for example by incorporation of active compound and excipients into a hard gelatin capsule. Alternatively, a semi-solid matrix of active compound and high molecular weight polyethylene glycol can be prepared and filled into a hard gelatin capsule; or a solution of active compound in polyethylene glycol or a suspension in edible oil, for example liquid paraffin or fractionated coconut oil can be prepared and filled into a soft gelatin capsule. Compound of Formula 1 and their pharmaceutically acceptable salts which are active when given parenterally can be formulated for intramuscular or intravenous administration.

A typical composition for intra-muscular administration will consist of a suspension or solution of active ingredient in an oil, for example arachis oil or sesame oil. A typical composition for intravenous administration will consist of a sterile isotonic aqueous solution containing, for example active ingredient, dextrose, sodium

chloride, a co-solvent, for example polyethylene glycol and, optionally, a chelating agent, for example ethylenediamine tetracetic acid and an anti-oxidant, for example, sodium metabisulphite. Alternatively, the solution can be freeze dried and then reconstituted with a suitable solvent just prior to administration.

Compounds of structure (1) and their pharmaceutically acceptable salts which are active on rectal administration can be formulated as suppositories. A typical suppository formulation will generally consist of active ingredient with a binding and/or lubricating agent such as a gelatin or cocoa butter or other low melting vegetable or synthetic wax or fat.

Compounds of Formula 1 and their pharmaceutically acceptable salts which are active on topical administration can be formulated as transdermal compositions. Such compositions include, for example, a backing, active compound reservoir, a control membrane, liner and contact adhesive.

The typical daily dose of a compound of Formula 1 varies according to 15 individual needs, the condition to be treated and with the route of administration. Suitable doses are in the general range of from 0.001 to 10 mg/kg bodyweight of the recipient per day.

Within this general dosage range, doses can be chosen at which the compounds of Formula 1 lower plasma cholesterol levels and raise metabolic rate 20 with little or no direct effect on the heart. In general, but not exclusively, such doses will be in the range of from lower doese (0.001 to 0.5 mg/kg) to higher doses (0.5 to 10 mg/kg).

In addition, within the general dose range, doses can be chosen at which the compounds of Formula 1 lower plasma cholesterol levels and have little or no effect 25 on the heart without raising metabolic rate. In general, but not exclusively, such doses will be in the range of from 0.001 to 0.5 mg/kg.

It is to be understood that the 2 sub ranges noted above are not mutually exclusive and that the particular activity encountered at a particular dose will depend on the nature of the compound of Formula 1 used.

Preferably, the compound of Formula 1 is in unit dosage form, for example, a tablet or a capsule so that the patient may self-administer a single dose. In general, unit doses contain in the range of from 0.05-100 mg of a compound of Formula 1. Preferred unit doses contain from 0.05 to 10 mg of a compound of Formula 1.

The active ingredient may be administered from 1 to 6 times a day. Thus daily doses are in general in the range of from 0.05 to 600 mg per day. Preferably, daily doses are in the range of from 0.05 to 100 mg per day. Most preferably from 0.05 to 5 mg per day.

5

EXAMPLES

EXAMPLE 1 - SYNTHESIS OF TR LIGANDS

Many TR ligands are known in the art, including T4 (thyroxine), T3, T2 and TS-9. See Jorgensen, Thyroid Hormones and Analogs, in *Hormonal Proteins and* 10 *Peptides, Thyroid Hormones* 107-204 (Choh Hao Li ed., 1978), incorporated by reference herein.

The syntheses of several TR ligands are described below.

Synthesis of TS1, TS2, TS3, TS4, TS5

TS1, TS2, TS3, TS4 and TS5 and analogs thereof can all be prepared by simple acylation of the nitrogen atom of any thyronine analog, including T3 (3,5,3'-triiodo-L-thyronine), T4 (thyroxine) and 3,5-diiodothyronine. TS1 and TS2 are synthesized by reacting T3 with Ph₂CHCO₂NHS (N-hydroxy succinimide-2,2-diphenylacetate) and C₁₆H₃₃CO₂NHS, respectively. TS3 is synthesized by reacting T3 with FMOC-Cl (fluorenylmethyloxycarbonylchloride). TS4 is synthesized by reacting T3 with tBOC₂O (tBOC anhydride or di-t-butyldicarbonate). TS5, which differs from TS1-4 by having a -H instead of an -I at the R'₃ position, is synthesized by reacting 3,5-diiodothyronine with tBOC₂O. The general reaction scheme for TS1, TS2, TS3, TS4 and TS5 is depicted in FIG. 11. It should be noted that in the reaction scheme, both TS5 and its precursor both have a hydrogen rather than an iodine at the R'₃ position.

Synthesis of TS6 and TS7

TS6 is synthesized by reacting TS5 with paranitrophenylisocyanate. TS7 is synthesized by reacting TS6 with TFA (trifluoroacetic acid), which cleaves the tBOC group. These reactions are simple organic synthesis reactions that can be performed by anyone of ordinary skill in the art. The synthetic scheme for TS6 and TS7 is diagrammed in FIG. 12.

Synthesis of TS8

TS8 is synthesized by reacting TS5 with Ph₂CHNH₂ (diphenylmethylamine) in the presence of triethylamine and any amide forming condensing reagent, such as TBTU (hydroxybenztriazoleuronium tetrafluoroborate) or HBTU (hydroxybenztriazoleuronium hexafluorophosphate). The synthesis scheme for TS8 is depicted in FIG. 13.

SYNTHESIS OF 3,5-DIIODO-3'ISOPROPYLTHYRONINE DERIVATIVES

For designing a class of antagonists, it is important to have a hydrophobic group at the 3' position as well as an extension at the 5' position. Preferred hydrophobic groups at the 3' position include: methyl, benzyl, phenyl, iodo, and heterocyclic structures. The synthesis of a 3,5-diiodo-3'-isopropyl-5'-substituted thyronine is described below. The example provided describes the specific steps for synthesizing the TS10 compound, but this general reaction scheme can be used by one of ordinary skill in the art to synthesize any number of 3,5,-diiodo-3'-isopropyl-5'-substituted thyronine derivatives, which are characterized by having an extension at the 5' position. Additional compounds of this class can be synthesized using known organic synthesis techniques.

The synthesis of TS10 is described below and is depicted in FIG. 14. Numbers used in the reaction scheme for TS10 indicating the reaction product for each step are in parentheses.

2-Formyl-6-isopropylanisole (1): 2-formyl-6-isopropylanisole (10.0 g, 61 mmol), as made by Casiraghi, *et al.* JCS Perkin I, 1862 (1980) (incorporated by reference), is added dropwise to a suspension of sodium hydride (3.7 g, 153 mmol) in 50 mL THF and 50 mL of DMF in a round bottom flask. The addition generates an exothermic reaction and formation of a gray solid. Methyl iodide (26.0 g, 183 mmol) is then added dropwise and the reaction mixture is stirred at room temperature for 5 hours. The reaction mixture is quenched with 20 mL of water, then poured into 500 mL of water, and is extracted with ether (2 x 300 mL). The ether layers are combined, washed with water (5 x 1000 mL), dried over magnesium sulfate and concentrated in vacuo to provide 10.2 g (94%) of the title compound, with the following ¹H NMR (CDCl₃) properties: d 10.30 (s, 1H), 7.63 (d, 1H, J=3 Hz), 7.50

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(d, 1H, J=3 Hz), 7.13 (t, 1H, J=3 Hz), 3.81 (s, 3H), 3.31 (heptet, 1H, J=7.5 Hz), 1.19 (d, 6H, J=7.5 Hz).

2-(2-Hydroxynonyl)-6-isopropylanisole (not shown in scheme):

5 Octylmagnesium chloride (8.4 mL, 16.9 mmol, 2.0 M) is added dropwise to a solution of 1 (1.5 g, 8.4 mmol) in 10 mL THF at -78°C. The reaction mixture is stirred for 2 hours with warming to room temperature. The reaction mixture is diluted with 50 mL ether and poured into 50 mL water. The ether layer is washed with brine (1 x 50 mL), dried over sodium sulfate, and concentrated in vacuo. Flash chromatography (silica 10 gel, 10% ether/hexane → 15% ether/hexane) provides 734 mg (30%) of the title compound with the following ¹H NMR (CDCl₃) properties: d 7.33-7.10 (m, 3H), 5.00 (br. s, 1H), 3.81 (s, 3H), 3.33 (heptet, 1H, J=7 Hz) 1.90-1.19 (m, 14H), 0.86 (t, 3H, J=6.5 Hz); HRMS (EI), found: 292.2404; calc'd: 292.2402.

2-nonyl-6-isopropylanisole (2): Compound 2 (663 mg, 2.3 mmol) is dissolved in solution of 5 mL ethanol and 5 mL acetic acid, and a spatula tip of palladium on carbon catalyst is added. The reaction mixture is then charged with hydrogen gas (using a simple balloon and needle) and the mixture is stirred at room temperature overnight. The next day, the reaction mixture is poured into ether (100 mL) and the ether layer is extracted with saturated sodium bicarbonate (3 x 100 mL). The ether layer is dried over sodium sulfate and concentrated *in vacuo* to provide 581 mg (91%) of (2) with the following ¹H NMR (CDCl₃) properties: d 7.14-7.00 (m, 3H), 3.75 (s, 3H), 3.36 (heptet, 1H, J=6.8 Hz), 2.63 (t, 2H, J=7.5 Hz), 1.68-1.15 (m, 14H), 0.86 (t, 3H, J=5.5 Hz); HRMS (EI), mass found: 276.2459; calculated: 276.2453.

Thyronine adduct (4): Fuming nitric acid (0.071 mL) is added to 0.184 mL acetic anhydride chilled to -5°C. Iodine (66 mg) is added to this mixture followed by trifluoroacetic acid (0.124 mL). This mixture is stirred for 1 hour with warming to room temperature, at which point all of the iodine is dissolved. The reaction mixture was then concentrated *in vacuo* to provide an oily semi-solid material. The residue was dissolved in 0.7 mL of acetic anhydride and cooled to -20°C. A solution of anisole (2) (581 mg, 2.1 mmol) in 1.2 mL acetic anhydride and 0.58 mL TFA is added dropwise. The reaction mixture is stirred at -20° for 1 hour, then stirred overnight with warming to room temperature. The reaction mixture is partitioned between water and methylene chloride. The methylene chloride layer is dried over sodium

sulfate and concentrated *in vacuo* to provide the iodonium salt (3) as an oil. This material is not purified or characterized, and is directly introduced into the coupling reaction.

N-Trifluoroacetyl-3,5-diiodotyrosine methyl ester (552 mg, 1.0 mmol) prepared according to the procedure of N. Lewis and P. Wallbank, *Synthesis* 1103 (1987) (incorporated by reference) and all of the crude iodonium salt (3) from above is dissolved in 5 mL of anhydrous methanol. Diazabicyclo[5.4.0]undecane (DBU) (183 mg, 1.2 mmol) and a spatula tip of copper-bronze are added and the resulting mixture is stirred at room temperature overnight. The next day, the reaction mixture is filtered, and the filtrate is concentrated *in vacuo*. The crude residue is purified by flash chromatography (silica gel, 10% ethyl acetate/hexane) to provide 30 mg (4%) of the protected thyronine adduct (4).

Deprotected thyronine (TS10): The protected thyronine 4 (30 mg, 0.04 mmol) is dissolved in a mixture of 2.25 mL acetic acid and 2.25 mL 49% hydrobromic acid.

15 The reaction mixture is heated to reflux for 5 hours. The reaction mixture is cooled to room temperature, and the solvents are removed *in vacuo*. Water is added to triturate the oily residue into a gray solid. This solid material is filtered, washed with water, and dried over P₂O₅ *in vacuo* to provide 24 mg (81%) of the title compound, TS10, with the following ¹H NMR (CDCl₃) properties: d 7.57 (s, 1H), 6.86 (s, 1H), 6.45 (s, 20 1H), 6.34 (s, 1H), 4.81 (m, 1H), 3.86 (s, 3H), 3.71 (s, 3H), 3.33-3.05 (m, 3H), 2.58-2.47 (m, 2H), 1.62-0.76 (m, 23H); MS (LSIMS): M⁺ = 817.0.

As mentioned above, this reaction scheme can be modified by one of ordinary skill in the art to synthesize a class of compounds characterized by 3,5-diiodo-3'isopropylthyronine derivatives, wherein (1) the 3' isopropyl group can be replaced with a hydrophobic group, including methyl, benzyl, phenyl, iodo, and heterocyclic structures, and (2) a wide variety of chemical structures can be incorporated at the 5' position, including alkyl groups, planar aryl, heterocyclic groups, or polar and/or charged groups.

The aldehyde (1) in the above reaction scheme is a versatile synthetic 30 intermediate which allows for the attachment of a variety of chemical moieties to the 5' position of the final thyronine derivative. In addition, a variety of chemical reactions can be used to attach the chemical moieties. These reactions are well known in the art and include organometallic additions to the aldehyde (including Grignard reagents, organolithiums, etc.), reductive amination reactions of the aldehyde with a

primary or secondary amine, and Wittig olefination reactions with a phosphorous ylid or stabilized phosphonate anion. Other possibilities include reduction of the aldehyde to a benzyl alcohol allowing for etherification reactions at the 5' position. As mentioned above, these methods allow for a wide variety of chemical structures to be incorporated at the 5' position of the final thyronine derivative, including alkyl groups, planar aryl, heterocyclic groups or polar and/or charged groups.

Synthesis of 3, 5-dibromo-4-(3',5'-diisopropyl-4'-hydroxyphenoxy) benzoic acid (Compound 11).

- (a) A mixture of 2,6-diisopropyl phenol (20 g, 0.11 mol), potassium carbonate (62 g, 0.45 mol), acetone (160 ml) and methyl iodide (28 ml, 0.45 mole) is refluxed for three days. The reaction mixture is filtered through celite, evaporated, dissolved in ether, washed twice with 1M sodium hydroxide, dried over magnesium sulphate and concentrated to afford 15.1 g (0.08 mol, 70%) of 2,6-diisopropyl anisole as a 20 slightly yellow oil.
- (b) Fuming nitric acid (12.4 ml, 265 mmol) is added dropwise to 31.4 ml of acetic anhydride which is cooled in a dry ice/carbon tetrachloride bath. Iodine 11.3 g, 44.4 mmol) is added in one portion followed by dropwise addition of trifluoroacetic acid (20.5 ml, 266 mmole). The reaction mixture is stirred at room temperature until all the iodine is dissolved. Nitrogen oxides are removed by flushing nitrogen into the vessel. The reaction mixture is concentrated, the residue is dissolved in 126 ml of acetic anhydride and is cooled in a dry ice/carbon tetrachloride bath. To the stirred solution 2,6-diisopropylanisole (51 g, 266 mmol) in 150 ml of acetic anhydride and 22.6 ml of trifluoroacetic acid is added dropwise. The reaction mixture is left to stand at room temperature over night and then is concentrated. The residue is taken up in 150 ml of methanol and treated with 150 ml of 10% aqueous sodium bisulfite solution and 1 liter of 2M sodium borotetrafluoride solution. After the precipitate aggregates, petroleum ether is added and the supernatant is decanted. The precipitate is triturated with petroleum ether, filtered, washed with petroleum ether and dried at room

temperature in vacuo. This affords 34 g (57 mmol, 65%) of bis(3,5-diisopropyl-4-methoxyphenyl)iodonium tetrafluoroborate as a white solid.

- (c) To a stirred solution of 3,5-dibromo-4-hydroxybenzoic acid (12 g, 40.5 mmol) in 250 ml of methanol, thionyl chloride (3 ml) is added dropwise. The reaction mixture is refluxed for five days, water is added and the precipitated product is filtered off. The residue is dissolved in ethyl acetate. From the aqueous phase, methanol is removed by concentration. The aqueous phase is then saturated with sodium chloride, and extracted with ethyl acetate. The combined organic phases are dried over magnesium sulphate, filtered and concentrated. This gives 12.5 g (40.5 mmol, 100%) of 3,5-dibromo-4-hydroxymethyl benzoate as a white crystalline solid.
- (d) The products obtained in steps b and c are reacted with each other according to the following protocol. To bis(3,5-diisopropyl-4-methoxyphenyl)iodonium tetrafluoroborate (2.86 g, 4.8 mmole) and copper bronze (0.42 g, 6.4 mmole) in 7 ml. of dichloromethane at 0°C is added dropwise a solution of 3,5-dibromo-4-hydroxymethyl benzoate (1.0 g, 3.2 mmole) and triethylamine (0.36 g, 3.5 mmole) in 5 ml of dichloromethane. The reaction mixture is stirred in the dark for eight days and then is filtered through celite. The filtrate is concentrated and the residue is purified by column chromatography (silica gel, 97:3 petroleum ether/ethyl acetate) to give 0.62 g (1.2 mmole, 39%) of 3,5-dibromo-4-(3',5'-diisopropyl-4'-20 methoxyphenoxy)methyl benzoate as a solid.
- (e) The product from step d (0.2 g, 0.4 mmole) is dissolved in 2 ml. dichloromethane, is put under nitrogen and is cooled at -40°C. To the stirred solution is added 1M BBr₃ (1.2 ml, 1.2 mmole) dropwise. The reaction mixture is allowed to reach room temperature and then is left over night. It is cooled to 0°C and then 25 hydrolyzed with water. Dichloromethane is removed by concentration and the aqueous phase is extracted with ethyl acetate. The organic phase is washed with 1M hydrochloric acid and brine. Then it is dried over magnesium sulphate, filtered and residue is chromatographed (silica, 96:3.6:0.4 concentrated. The dichloromethane/methanol/acetic acid) producing 93 mg (0.2 mmole, 51%) of 3,5-30 dibromo-4-(3',5'-diisopropyl-4'-hydroxyphenoxy)benzoic acid as a white solid. H nmr (CDCl₃) 8 1.23 (d, 12H, methyl), 3.11 (m, 2H, CH), 6.50 (s, 2H, 2,6-H) 8.33 (s, 2H, 2',6'-H).

Synthesis of addition ligands are described in U.S. Serial No. 08/877,792, filed June 18, 1997 which is herein incorporated in its entirety by reference.

TABLE 2 and **FIG. 15** depict the structures of several TR ligands in reference to Formula I.

5

TABLE 2

Cmpd	R ₃	R4	R ₅	R' ₃	R' ₄	R's	R ₁
*T;	-i	-0-	-1	-I	-OH	-Н	-CH₂CH(NH₂)CO₂H
*T₄	-i	-0-	-l	-1	-OH	-I	-CH₂CH(NH₂)CO₂H
TS1	-l	-0-	-l	-I	-OH	-Н	-CH₂CH[NHCOCH∳₂]CO₂H
TS2	-1	-0-	-1	-[-OH	-Н	-CH ₂ CH[NHCO(CH ₂) ₁₅ CH ₃]CO ₂ H
TS3	-1	-0-	-1	-i	-OH	-H	-CH₂CH[NH-FMOC]CO₂H
TS4	-I	-0-	-1	-1	-OH	-H	-CH₂CH[NH-tBOC]CO₂H
TS5	-1	-0-	-1	-H	-OH	-H	-CH₂CH[NH-tBOC]CO₂H
TS6	-1	-0-	-I	-H	-OC(O)NH=Ø _p NO ₂	-H	-CH₂CH[NH-tBOC]CO₂H
TS7	-I	- 0-	i-	-I	- OC(O)NH=NHØNO₂	-H	-CH₂CH(NH₂)CO₂H
TS8 .	-l	-0-	-1	-H	-NH-CHØØ	-Н	-CH ₂ CH[NH-tBOC]CO ₂ H
TS9	1-	-0-	-[-IsoPr	-ОН	-Н	-CH₂CH(NH₂)CO₂H
TS10	-I	-0-	-1	-IsoPr	-ОН	-(CH) ₈ - CH ₃	-CH₂CH(NH₂)CO₂H

Prior Art Compound

-Ø:

phenyl

-ØpNO₂:

para nitro phenyl

10

EXAMPLE 2 - RECEPTOR BINDING ASSAYS OF TR LIGANDS

To test the ability of synthesized TR ligands to bind to a thyroid receptor (TR), the binding affinity of a TR ligand for TR is assayed using TR's prepared from rat liver nuclei and [125]T₃ as described in J.D. Apriletti, J.B. Baxter, and T.N. Lavin, J. Biol. Chem., 263: 9409-9417 (1988). The apparent Kd's are calculated using the method described by Apriletti (1995) and Apriletti (1988). The apparent Kd's are presented in TABLE 3. The apparent Kd's (App.Kd) are determined in the presence

of the sample to be assayed, 1 nM [¹²⁵I]T₃, and 50Tg/ml core histones, in buffer E (400 mM KCl, 200 mM potassium phosphate, pH 8.0, 0.5 mM EDTA, 1 mM MgCl₂, 10% glycerol, 1 mM DTT) in a volume of 0.21 ml. After incubation overnight at 4°C, 0.2 ml of the incubation mixture is loaded onto a Quick-Sep Sephadex G-25 column 5 (2.7 x 0.9 cm, 1.7 ml bed volume) equilibrated with buffer E. The excluded peak of protein-bound [¹²⁵I]T₃ is eluted with 1 ml of buffer E, collected in a test tube, and counted. Specific T₃ binding is calculated by subtracting nonspecific binding from total binding.

TABLE 3

Compound	App.Kd(nM)	Coactivation Assay RIP-140	EC ₅₀ (M)
T ₃	0.06	+	10 ⁻¹⁰
T ₄	2	+	10-9
TS1	4	+	10-7
TS2	1400	nd	nd
TS3	4	+	10-8
TS4	8	+	nd
TS5	. 220	+	10-6
TS6	>10000	nd	nd
TS7	260	+	10 ⁻⁷
TS8	6000	nd	nd
TS9	1	+	10 ⁻¹⁰
TS10	400	+	10 ⁻⁶

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+: RIP-140 Binding

-: RIP-140 Binding

nd: Not Determined

EXAMPLE 3 - INCREASED NUCLEAR PROTEIN COACTIVATION BY TR LIGANDS

To test the ability of TR ligands to activate the binding of TR to the nuclear activation protein RIP-140 (a nuclear protein that can bind to nuclear receptors, such as the estrogen receptor), a TR ligand is liganded to TR and then incubated with RIP-140 as described in V. Cavailles, et al., EMBO J., 14(15):3741-3751 (1995), which is incorporated by reference herein. In this assay, ³⁵S-RIP-140 protein binds to liganded TR but not unliganded TR. Many TR ³⁵S ligands can activate RIP-140 binding as shown in **TABLE 3**.

10 Example 4 - TR LIGAND BINDING AND TR ACTIVATION IN CULTURED CELLS

To test TR activation of transcription in a cellular environment, TR ligands are assayed for their ability to activate a reporter gene, chloramphenicol transferase ("CAT"), which has a TR DNA binding sequence operatively linked to it. Either GC or L937 cells (available from the ATCC) can be used, respectively). In such assays, a 15 TR ligand crosses the cell membrane, binds to the TR, and activates the TR, which in turn activates gene transcription of the CAT by binding the TR DNA binding region upstream of the CAT gene. The effective concentration for half maximal gene activation (EC₅₀) is determined by assaying CAT gene activation at various concentrations as described herein and in the literature. The results of CAT gene 20 activation experiments are shown in **TABLE 3**.

CAT GENE ACTIVATION ASSAYS

Functional response to thyroid hormone (3,5,3'-triiodo-L-thyronine, T₃) and TR ligands is assessed either in a rat pituitary cell line, GC cells, that contain 25 endogenous thyroid hormone receptors (TRs) or U937 cells that contain exogenous TRs expressed as known in the art. GC cells are grown in 10-cm dishes in RPMI 1640 with 10% newborn bovine serum, 2 mM glutamine, 50 units/ml penicillin and 50 Tg/ml streptomycin. For transfections, cells are trypsinized, resuspended in buffer (PBS, 0.1% glucose) and mixed with a TREtkCAT plasmid (10 mg) or phage in 0.5 ml buffer (15±5 million cells) and electroporated using a Bio-Rad gene pulser at 0.33 kvolts and 960 mF. The TREtkCAT plasmid contains two copies of a T₃ response element (AGGTCAcaggAGGTCA) cloned in the Hind III site of the pUC19 polylinker immediately upstream of a minimal (-32/+45) thymidine kinase promoter

linked to CAT (tkCAT) coding sequences. After electroporation, cells are pooled in growth medium (RPMI with 10% charcoal-treated, hormone stripped, newborn bovine serum), plated in 6-well dishes and treated with either ethanol or hormone. CAT activity is determined 24 hours later as described D. C. Leitman, R. C. J. 8 Ribeiro, E. R. Mackow, J. D. Baxter, B. L. West, J. Biol. Chem. 266, 9343 (1991), which is incorporated by reference herein.

EFFECT OF TS-10 ON THE TRANSCRIPTIONAL REGULATION OF THE DR4-ALP REPORTER GENE IN THE PRESENCE OF ABSENCE OF T3.

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Characteristics of the TRAF cells: TRAFa1 are CHO K1 cells stably transformed with an expression vector encoding the human thyroid hormone receptor α1 and a DR4,ALP reporter vector; TRAFb1 are CHO K1 cells stably transformed with an expression vector encoding the human thyroid hormone receptor β1 and a 15 DR4-ALP reporter vector.

Interpretation of the effect of compound TS-10 on the transcriptional regulation of the DR4-ALP reporter gene in the presence or absence of T3.

TRAFa1 reporter cells: TS-10 alone (open circles) induces a partial activation of the expression of the ALP reporter protein amounting to approximately 27% of the maximal effect by the natural thyroid hormone T3. In the presence of T3 (filled circles), TS-10 has a weak antagonistic effect. The EC50 concentration for the agonistic effect of TS-10 and the EC50 concentration for its T3 antagonistic effect, respectively, is indicated in FIG. 18.

In FIG. 18, open and filled circles with dotted lines show the dose-dependent effect of TS-10/T3 on the toxicity marker (MTS/PMS), reduction of tetrazolium salt in the mitochondria, displayed on the right y-axis as optical density. There is no obvious toxic effect of TS-10 on the MTS-PMS marker but there is a clear effect on the morphology of the cells, as can be seen under the light microscope, at the highest concentration of TS-10 (32 mM) both in the absence and presence of T3, respectively (not shown in the figure).

TRAFb1 reporter cells: TS-10 alone (open circles) induces a partial activation of the expression of the ALP reporter protein amounting to approximately 35% of the maximal effect by T3. The EC50 concentration for the agonistic effect of 5 TS-10 is indicated in FIG. 19. In the presence of T3 (filled circles), TS-10 shows, if anything, a slight potentiation of the T3 effect on the expression of the ALP reporter protein. The T3 inhibitory effect of TS-10 at its highest concentration used (32 mM) is a toxic effect rather than T3 antagonism.

In **FIG. 19**, open and filled circles with dotted lines show the dose-dependent effect of TS-10/T3 on the toxicity marker (MTS/PMS), reduction of tetrazolium salt in the mitochondria, displayed on the right y-axis as optical density. There is no obvious toxic effect of TS-10 on the MTS-PMS marker but a clear effect on the morphology of the cells can be observed, under the light microscope, at the highest concentration of TS-10 (32 mM) both in the absence and presence of T3, respectively (not shown in the figure).

HepG2 (HAF18) reporter cells: TS-10 alone (open circles) induces a partial activation of the expression of the ALP reporter protein amounting to slightly more than 50% of the maximal effect by T3. The EC50 concentration for the agonistic effect of TS-10 is indicated in FIG. 20. In the presence of T3 (filled circles), TS-10 shows no effect i.e. no T3 antagonism nor potentiation/additive effect to T3. Open and filled circles with dotted lines show the dose-dependent effect of TS-10/T3 on the toxicity marker (MTS/PMS), reduction of tetrazolium salt in the mitochondria, 25 displayed on the right y-axis as optical density. There is no obvious toxic effect of TS-10 on the MTS/PMS marker or on the morphology of the cells, as can be observed using a light microscope, at any concentration of TS-10/T3 used.

Example 5 - Comparisons of Human TR-α and Human TR-β

Competition for [125] T₃ binding to TR LBD by T₃ and Triac

The drug, Triac, is a thyroid hormone agonist. Triac is 3,5,3'-triiodothyroacetic acid and is described in Jorgensen, Thyroid Hormones and Analogs in *Hormonal Proteins and Peptides, Thyroid Hormones* at 150-151 (1978). Another

compound that can be used in place of Triac is 3,5-diiodo-3'-isopropylthyroacetic acid. Competition assays are performed to compare the displacement of $[^{125}I]T_3$ from binding with human TR- α LBD or human TR- β LBD by unlabeled T_3 or Triac. The results of such assays are depicted in **FIG. 16**.

5 Standard binding reactions are prepared containing 1 nM [¹²⁵I]T₃, 30 fmol of human TR-α (empty symbols) or β (solid symbols), and various concentrations of competing unlabeled T₃ (circles) or Triac (triangles). Assays are performed in duplicate.

10 Competition for [125I]T₃ binding to variant TR LBD by T₃, Triac and GC-1

The following assays residues involved in selective binding among TR isoforms. Competition assays are performed to compare the displacement of [125]T]₃ from binding with wild-type human TR-α LBD or human TR-β LBD, to a variant form of the TR LBDs by unlabeled T₃, Triac or GC-1. A variant TR-α or TR-β is constructed by substituting an amino acid found in the corresponding position of the other TR isoform. For example, asparagine 331 in human TR-β corresponds to serine 277 in human TR-α. To test binding specificity contributed by this position, a variant human TR-β is constructed that contains asparagine 331 substituted with a serine residue (designated Asn331Ser or N331S). Binding assays are described in *Apriletti* 20 *et al.* (Protein Expression and Purification 6:363-370 (1995)). The results of such assays are depicted in FIG. 27, and summarized in Table 4 below.

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TABLE 4	
Effect of TR-β Substitution N331S on Binding Affini	ty

Ligand	Native TR-α	Native TR-β	Mutant TR-β
T3 ·	20 pM	60 pM	100 pM
T4	600	3000	ND
Triac	20	20	100
IpBr ₂	17	ND	ND
Dimit	6000	8000	ND
ĢC-1	200	40	400

Competition curves comparing wildtype TR-β versus the variant TR-β N331S for 5 binding T3, Triac or GC-1 show that the affinity of the mutant receptor for Triac was reduced to approximately the same as for T3 (vs. 3-fold greater in wild type) so that the relative affinities are similar to wild-type TR-α. The affinity for GC-1 was also reduced to several fold less than T3, as is seen with TR-α.

Comparison of the affinity of TR- β variant N331S to the native TRs for 10 selected ligands is as follows:

Native TR-α for various ligands (T3, T4, Triac, IpBr2, Dimit, GC-1):

$$IpBr_2$$
. > Triac \cong T3 > GC-1 > T4 > Dimit

Native TR-B (T3, T4, Triac, Dimit, GC-1)

Triac > GC-1
$$\geq$$
 T3 > T4 > Dimit

15 Variant TR-β (N331S) (T3, Triac, GC-1)

Triac \cong T3 > GC-1.

Scatchard Analysis of [125I]T₃ Binding to TR

Human TR-α (left panel) or human TR-β (right panel) is assayed for T₃ 20 binding in the presence of increasing concentrations of [¹²⁵I]T₃. The apparent equilibrium dissociation constant (20 pM for I and 67 pM for β) is calculated by linear regression analysis and is depicted in **FIG. 17.**

3, 5-DIBROMO-4-(3',5'-DIISOPROPYL-4'-HYDROXYPHENOXY) BENZOIC ACID IS A TR-α SELECTIVE SYNTHETIC LIGAND.

3, 5-dibromo-4-(3',5'-diisopropyl-4'-hydroxyphenoxy) benzoic acid (Compound 11), the structure of which is drawn above, is assayed for binding to the two different isoforms of the TR, TR-α and TR-β. Compound 11 exhibits an IC50 of 1.6 TM for binding to TR-α and an IC50 of 0.91 TM for binding to TR-β. Assays for determining selective binding to the TR-α or TR-β LBD can include reporter assays, 15 as described herein. See also Hollenberg, et al., J. Biol. Chem., (1995) 270(24):14274-14280.

Example 6 - Preparation and Purification of a TR-α LBD

Rat TR-α LBD, residues Met122 - Val410, is purified from *E. coli* ("LBD-20 122/410"). The expression vector encoding the rat TR-α LBD is freshly transfected into *E. coli* strain BL21(DE3) and grown at 22°C in a 50-liter fermenter using 2x LB medium. At an A₆₀₀ of 2.5-3, IPTG is added to 0.5 mM and growth is continued for 3 h before harvesting. The bacterial pellet is quickly frozen in liquid nitrogen and stored at -70°C until processed. Extraction and purification steps are carried out at 25 4°C. The bacteria are thawed in extraction buffer (20MM Hepes, pH 8.-, 1 mM EDTA, 0.1% MTG, 0.1 mM PMSF, and 10% glycerol) at a ratio of 10 ml buffer/g bacteria. Bacteria are lysed by incubation for 15 min. with 0.2 mg/ml lysozyme and sonicated at maximum power while simultaneously homogenized with a Brinkmann homogenizer (Model PT 10/35 with generator PTA 35/2) until the solution loses its viscosity. After centrifugation for 10 min at 10,000 g, the supernatant is adjusted to 0.4 M KCl, treated with 0.6% PEI to precipitate fragmented DNA, and centrifuged for 10 min at 10,000 g. The precipitate with 50% ammonium sulfate and centrifuged for 10 min at 10,000 g. The precipitate is

resuspended with buffer B (20 mM Hepes, pH 8.0, 1 mM EDTA, 1 mM DTT, 0.1 mM PMSF, 0.01% Lubrol, and 10% glycerol) to a final conductivity of 9 mS/cm (approx. 0.7 M ammonium sulfate) and centrifuged 1 h at 100,000g. The supernatant is frozen in liquid nitrogen and stored at -70°C.

The crude extract is thawed, bound with a tracer amount of [¹²⁵I]T₃, and loaded directly onto a phenyl-Toyopearl hydrophobic interaction column (2.6 x 18 cm, 95 ml bed volume) at 1.5 ml/min. The column is eluted with a 2-h gradient from 0.7 ammonium sulfate, no glycerol to no salt, 20% glycerol in buffer C (20 mM Hepes, pH 8.0, 0.5 mM EDTA, 1 mM DTT, 0.2 mM PMSF). The rat TR-α LBD prebound to tracer [¹²⁵I]T₃ (less than 0.005% of total rat TR-α LBD) is detected using a flow-through gamma emission detector, whereas unliganded rat TR-I LBD is assayed by postcolumn [¹²⁵I]T₃ binding assays (described herein).

The phenyl-Toyopearl unliganded rat TR-α LBD peak fractions are pooled, diluted with buffer B to a conductivity of 0.5 mS/cm (equivalent to approx. 20 mM 15 ammonium sulfate), loaded onto a TSK-DEAE anion-exchange column (2 x 15 cm, 47 ml bed volume) at 4 ml/min, and eluted with a 60-min gradient from 50 to 200 mM NaCl in buffer B.

The unliganded rat TR-α LBD peak fractions from TSK-DEAE are pooled, diluted twofold with buffer B, loaded at 0.75 ml/min on a TSK-heparin HPLC column 20 (0.8 x 7.5 cm, 3 ml bed volume), and eluted with a 50 to 400 mM NaCl gradient in buffer B.

The pool of unliganded rat TR-α LBD peak fractions from the TSK-heparin column is adjusted to 0.7 M ammonium sulfate, loaded at 0.75 ml/min on a TSK-phenyl HPLC column (0.8 x 7.5 cm, 3 ml bed volume), and eluted with a 60-min gradient from 0.7 M ammonium sulfate without glycerol to no salt with 20% glycerol in buffer C. The fractions containing unliganded rat TR-α LBD are pooled and incubated with a five fold excess of hormone for 1 h, the salt concentration is adjusted to 0.7 M ammonium sulfate, and the sample is reloaded and chromatographed on the same column as described above.

EXAMPLE 7 - CRYSTALLIZATION OF LIGANDED TR-α LBD

Material from a single LBD-122/410 preparation is divided into batches, and quantitatively bound with one of the following ligands: Dimit, T₃, or Triac IpBr₂ (3,5dibromo-3'isopropylthyronine) for the final purification step.

To maintain full saturation of rat TR-α LBD with a ligand, and to prepare the complex for crystallization, the ligand-bound rat TR-α LBD is concentrated and desalted in an Amicon Centricon-10 microconcentrator (McGrath et al, *Biotechniques*, (1989) 7:246-247, incorporated by reference herein), using 10 mM Hepes (pH 7.0), 3.0 mM DTT, and 1.0 nM to 10 nM ligand.

Factorial crystallization screening trials (Jancarik & Kim, J. Appl. Crystallogr. 10 (1991) 24:409-411, incorporated by reference herein) are carried out for rat TR-α LBD bound to selected ligands using hanging-drop vapor diffusion at 17°C (with 1 µl protein solution, 1 µl precipitant solution and a 0.5 ml reservoir using silanized coverslip: (McPherson, Preparation and Analysis of Protein Crystals (1982), 15 incorporated by reference herein). Rat TR-α LBD is not stable at 4°C and is stored at -80°C, where it maintains its avidity for hormone and its crystallizability for approximately two to three months. These procedures are carried out as described in McGrath, M.E. et al., J. Mol. Biol. (1994) 237:236-239 (incorporated by reference). Crystals are obtained in condition 21 of the screening trials (Jancarik & Kim 1991) 20 and conditions are then optimized. Wedge-shaped crystals are reproducibly obtained with hanging-drop vapor fusion at 22°C with 15% 2-methyl-2,4-pentanediol (MPD), 0.2 M ammonium acetate and 0.1 M sodium cacodylate (pH 6.7), 3 mM DTT, with 2 μl protein solution, 1 μl precipitant solution and a 0.6 ml reservoir using silanized coverslip, and with 8.7 mg/ml (Dimit), 5.5 mg/ml (IpBr₂), 5 mg/ml (Triac), or 2.3 25 mg/ml (T₃) over a period of three days. Under these conditions, diffraction quality crystals (dimension 0.5 x 0.2 x 0.0075 mm³) can be grown at ambient temperature (22°C). The best crystals have a limiting dimension of approximately 100 Tm and are obtained at a protein concentration between 2.3 and 8.7 mg/ml in the presence of 3 mM DTT. The crystals are of the monoclinic space group C2, with one monomer in 30 the asymmetric unit.

Example 8 - Crystallization of Human TR- β LBD Complexed with T3, Triac, or GC-1

Human TR-β LBD complexed with T₃, Triac, or GC-1 are purified according to the same procedures described above for the rat TR-α LBD, with the following 5 modifications.

The expression of human TR-β LBD differs from the rat TR-α LBD in that the human TR-β LBD residues extend from the amino acid at position 716 through the amino acid at position 1022, according to the amino acid numbering scheme for the various nuclear receptor LBDs depicted in **FIG. 3. FIG. 3** illustrates a numbering scheme applicable to all of the nuclear receptors listed as well as to any additional homologous nuclear receptors. The vertical lines on **FIG. 3** at position 725 and at position 1025 delineate the preferred minimum amino acid sequence necessary to obtain adequate binding of ligand. The amino acid sequence from position 716 to position 1022 according to the numbering scheme of **FIG. 3** corresponds to the amino 15 acid positions 202 to 461 according to the conventional numbering of the amino acid sequence of human TR-β which is publicly available. Also, the human TR-β LBD is expressed with a histidine tag, as described in Crowe *et al.*, *Methods in Molecular Biology* (1994) 31:371-387, incorporated by reference herein.

The purification of human TR-β LBD is the same as that described above for the rat TR-α LBD with the following exceptions. First, before the purification step using the hydrophobic interaction column, a step is added in which the expressed human TR-β LBD is purified using a nickel NTA column (commercially available from Qiagen, Chatsworth, CA) according to manufacturer's instructions, and eluted with 200 mM imidazole. The second difference is that in the purification of the human TR-β LBD, the purification step using a heparin column is omitted.

The crystallization of human TR-β LBD bound to T₃, Triac or GC-1 is as follows. Crystals are obtained in condition 7 of the factorial screen using hanging drops as before at ambient temperature (22°C) using the factorial crystallization screening trials of Jancarik & Kim (1991) and using the commercially available product from Hampton Research, Riverside). The following are optimum conditions: hexagonal bipyrimidal crystals are grown at 4°C for 2-3 days from hanging drops containing 1.0-1.2 M sodium acetate (pH unadjusted) and 0.1 M sodium cacodylate (pH 7.4), 3 mM DTT, with either a 1 μl protein solution, 1 μl precipitant solution or 2

µl protein solution. 1 µl precipitant solution and a 0.6 ml reservoir using silanized coverslip, at a protein concentration of 7-10 mg/ml. The best crystals have a limiting dimension of 200 μm. The following are optimum conditions for crystallization of the TR-β LBD with GC-1: hexagonal bipyrimidal crystals are grown at 4°C for 2-3 days from hanging drops containing 0.8-1.0M sodium acetate (pH unadjusted), 50-200nM sodium succinate, and 0.1M sodium cacodylate (pH 7.2), 3mM DTT, 1 µl protein solution, 1 µl precipitant solution and a 0.6ml reservoir using silanized coverslip, at a protein concentration of 7-10 mg/ml. The best crystals have a limiting dimension of 200μM. The unit cell dimensions are cell length a=b=68.73, cell length 10 c=130.09. The unit cell angles are α=90°, β=90°, γ=120°.

The crystal system for human TR- β LBD bound to T₃, Triac or GC-1 is trigonal with the space group p3₁21. The unit cell dimensions are cell length a = cell length b = 68.448 angstroms, cell length c = 130.559 angstroms. The angles are α = 90°, β = 90°, gamma = 120°.

15

Example 9 - Determination of Liganded TR- α LBD and TR- β Crystal Structures

Data from each cocrystal (Rat TR-α LBD with Dimit, T3 and IpBr2; Human TR-β LBD with Triac and GC-1) is measured on a Mar area detector at Stanford 20 Synchrotron Radiation Laboratory beamline 7-1 (λ = 1.08 angstroms) using 1.2° oscillations. Data from the cocrystal of the hTR-β LBD with Triac is measured on a Mar area detector at Stanford Synchrotron Radiations Laboratory beamline 7-1 (λ = 1.08 angstroms) using 1.0 oscillations. Data from the cocrystal of the hTR-β LBd with GC-1 is measured on a R-axis II area detector on a Rigaku rotating Cu anode 25 (50kV, 300mA). The crystals are transferred into a cryosolvent containing 1.2M sodium acetate, 0.1M sodium cacodylate, adn 15% glycerol followed by a second transfer into 30% glycerol, then flash frozen in liquid nitrogen. An orientation matrix for each crystal is obtained using DENZO. The reflections are integrated with DENZO (commercially available from Molecular Structure Corp., The Woodlands, 30 Texas) and are scaled with SCALEPACK (as described in Otwinowski, Z, *Proceedings of the CCP4 Study Weekend: "Data Collection and Processing."* 56-62 (SERC Daresbury Laboratory, Warrington, UK 1993) incorporated by reference).

For rTR-α cocrystals, data from the T₃ cocrystal is measured with the b* axis approximately parallel with the spindle. The crystals are flash frozen at -178°C in a nitrogen gas stream with the MPD mother liquor serving as the cryosolvent. An orientation matrix for each crystal is determined using REFIX (Kabsch, W., J. Appl. 5 Crystallogr. (1993) 26:795-800 incorporated by reference). Reflections are integrated with DENZO, and are scaled with SCALEPACK.

For the T₃ data set, Bijvoet pairs are kept separate, and are locally scaled using MADSYS (W. Hendrickson (Columbia University) and W. Weis (Stanford University)).

Cocrystals prepared from the three isosteric ligands are isomorphous. MIR 10 analysis is performed using programs from the CCP4 suite (Collaborative Computational Project, N.R. Acta Crystallogr. (1994) D50:760-763, incorporated by reference herein). Difference Pattersons is calculated for both T₃ and IpBr₂, taking the Dimit cocrystal as the parent. The positions of the three iodine atoms in the T₃ 15 difference Patterson are unambiguously determined from the Harker section of the density map as peaks of 11[above background. The positions for the two bromine atoms in the IpBr2 cocrystals, are located independently, as peaks 8[above the noise level. Phases for the LBD-122/410 are calculated from the solution to the IpBr₂ difference Patterson, and are used to confirm the location of the unique third iodine of 20 the T₃ cocrystal. Halogen positions are refined with MLPHARE, including the anomalous contributions from the iodine atoms (Otwinowski, Z, Proceedings of the CCPR Study Weekend 80-86 (SERC Daresbury Laboratory, Warrington, UK 1991)). The MIRAS phases are improved through solvent flattening/histogram matching using DM (Cowtan, K., Joint CCP4 and ESF-EACBM Newsletter on Protein 25 Crystallography (1994) 31: 34-38, incorporated by reference herein).

A model of the LBD-122/410 with Dimit bound is built with the program O from the solvent flattened MIRAS 2.5 angstrom electron density map (Jones et al., Acta Crystallogr. (1991) A 47:110-119, incorporated by reference herein). The initial model, without ligand, (Rcryst = 40.1%), is refined using least-squares protocols with XPLOR. The Dimit ligand is built into unambiguous Fo-Fc difference density during the following round. Subsequent refinement employs both least-squares and simulated annealing protocols with XPLOR (Brunger et al., Science (1987) 235:458-460), incorporated by reference herein). Individual atomic B-factors are refined

isotropically. As defined in PROCHECK, all residues are in allowed main-chain torsion angle regions as described in Laskowski *et al.*, *J. Appl. Crystallogr.*, (1993) 26:283-291, incorporated by reference herein. The current model is missing 34 residues (Met₁₂₂-Gln₁₅₆) at the N-terminus, and 5 residues (Glu₄₀₆-Val₄₁₀) at the C-5 terminus.

In addition, the following residues are not modeled beyond Cβ due to poor density: 184, 186, 190, 198, 206, 209, 240, 301, 330, 337, 340, 343, 359, and 395. The average B-value for protein atoms is 34.5 Å². The final model consists of the LBD-122/410, residues Arg₁₅₇-Ser₁₈₃, Trp₁₈₅-Gly₁₉₇, Ser₁₉₉-Asp₂₀₆ and Asp₂₀₈-Phe₄₀₅; 10 three cacodylate-modified cysteines: Cys₃₃₄, Cys₃₈₀ and Cys₃₉₂; and 73 solvent molecules modeled as water (2003 atoms).

*
$$R_{sym} = 100 \times \Sigma_{hkl} \Sigma_i \mid I_i - I \mid / \Sigma_{hkl} \Sigma_i I_i$$

$$\dagger R_{der} = 100 \times \Sigma_{hkl} \mid F_{PH} - F_H \mid / \Sigma_{hkl} \mid F_P \mid$$

The occupancy for the two bromine sites is set to 35 electrons. The occupancies of the 15 iodine sites are relative to this value.

§Phasing power = $\langle FH \rangle$, $/ \langle \epsilon \rangle$, where $\langle FH \rangle$ is the mean calculated heavy atom structure factor amplitude and $\langle \epsilon \rangle$ is the mean estimated lack of closure.

4Rcullis = $\langle \in \rangle / \langle iso \rangle$, where $\langle \in \rangle$ is the mean estimated lack of closure and $\langle iso \rangle$ is the isomorphous difference.

20 ¶Rcryst = 100 x Σ_{hkl} $|F_0 - F_c|$ / Σ_{hkl} $|F_0|$ where F_0 and F_c are the observed and calculated structure factor amplitudes (for data $F/\sigma > 2$). The Rfree was calculated using 3% of the data, chosen randomly, and omitted from the refinement.

§ Correlation coefficient =
$$\Sigma_{hkl}$$
 ($|F_o| - |F_o|$) x ($|F_c| - |F_c|$)/ Σ_{hkl} ($|F_o| - |F_o|$)²x Σ_{hkl} ($|F_c| - |F_c|$)²

25

Example 10. Phasing of the rTR- α LBD and hTR- β LBD complex with Triac

Due to the possible non-isomorphism of the rTRα LBD complex with Triac, a molecular replacement solution is determined using AMORE (Navaza, J., Acta 30 Crystallographica Section A-Fundamentals of Crystallography (1994) 50:157-63 from a starting model consisting of rTRI LBD complex with T₃, but with the ligand, all water molecules, and the following residues omitted: Asn 179, Arg228, Arg262, Arg266, and Ser 277. Strong peaks are obtained in both the rotation and translation

searches, with no significant (> 0.5 times the top peak) false solutions observed (Table 6). Strong positive density present in both the anomalous and conventional difference Fourier maps confirm the solution. Maps are calculated using sigma-A weighted coefficients output by REFMAC (Murshudov, et al. "Application of 5 Maximum Likelihood Refinements," in Refinement of Protein Structures, Proceedings of Daresbury Study Weekend (1996)) after 15 cycles of maximum likelihood refinement. Triac, the omitted residues, and water molecules 503, 504, 534 (following the numbering convention for the TR complex with T3) are built into the resulting difference density using O (Jones et. al.); the conformations of these residues are further confirmed in a simulated-annealing omit map (Brunger et. al.). The complete model is then refined using positional least-squares, simulated annealing, and restrained, grouped B factor refinement in XPLOR to an Reryst of 23.6% and an Rfree of 24.1%

Phasing of a related LBD using the structure of the rTR-α LBD is conducted 15 as follows. A molecular replacement solution for the hTR-β LBD complex with Triac is determined using AMORE from a starting model consisting of the rTR-a LBD complexed with T3, but with the ligand and all water molecules omitted. Strong peaks are obtained in both the rotation and translation searches, with no significant (>0.5 times the top peak) false solutions (Table 7). Strong positive density present in 20 both the anomalous and conventional difference Fourier maps confirm the solution. Initial maps are calulated using sigma-A weighted coefficients output by REFMAC after 9 cycles of maximum likelihood refinement. The real-space fit for each residues was calculated using OOPS (Kleywegt, GJ and Jones, TA, OOPS-a-daisy, ESF/CCP4 Newsletter 30, June 1994, pp. 20-24) and the residues with a real-space fit less than 2 25 standard deviations below the mean removed: Ala253-Lys263; Glu245-Leu250. To reduce bias, the following residues were modeled as alanine: Arg282, Arg316, Arg 320, Asn 331. Cycles of rebuilding and positional least-squares, simulated annealing, and restrained, grouped B factor refinement with XPLOR produce a model with an R_{cryst} of 25.3 and an R_{free} of 28.9%. The final model consists of hTR-β LBD residues 30 Glu202-Gln252, Val264-Glu460; three cacodylate-modified cysteines with the cacodylate moeity modeled as free arsenic: Cys294, Cys298, Cys388, and Cys434; and 35 solvent molecules modeled as water.

EXAMPLE 11. CONNECTING QSAR WITH STRUCTURE IN THE THYROID HORMONE RECEPTOR

The conclusions of classic thyroid hormone receptor quantitative structureactivity relationships may be summarized as follows:

- 5 1) the R₄'-hydroxyl group functions as a hydrogen bond donor;
 - 2) the amino-propionic acid interacts electrostatically through the carboxylate anion with a positively charged residue from the receptor;
 - 3) the preferences of R_3/R_5 substituent are I>Br>Me>>H;
 - 4) the preferences of the R₃'-substituent are Ipr>I>Br>Me>>H.
- 10 The structure of the thyroid hormone receptor ligand binding domain complexed with the agonists T3, IpBr₂, Dimit, Triac, and GC1 as provided herein, permits:
 - the identification of receptor determinants of binding at the level of the hydrogen bond;
 - the association of these determinants with the predictions of classic thyroid hormone receptor QSAR; and
 - 3) prediction as to which determinants of binding are rigid, and which are flexible, for both the ligand and the receptor.

This classification for the agonists of the type (R_1 =amino-propionic, acetic acid; R_3,R_5 =I,Br,Me; R_3 '=Ipr,I) is given below (for the representative ligand T_3);

20

15

F = Fiducial (always satisfied)

A = Adjustable

30

Based upon the methods and data described herein, the following is an embodiment of the computational methods of the invention, which permit design of nuclear receptor ligands based upon interactions between the structure of the amino acid residues of the receptor LBD and the four different ligands described herein. The

small molecule structures for the ligands can be obtained from Cambridge Structural Database (CSD), and three dimensional models can be constructed using the methods described throughout the specification. The following are factors to consider in designing synthetic ligands:

- 1) Histidine 381 acts as a hydrogen bond acceptor for the R₄' hydroxyl, with the optimal tautomer maintained by water molecules. See FIG. 23 and FIG 24. Histidine is the only hydrophilic residue in this hydrophobic pocket that surrounds the R₄' substituent. Histidine can be either a hydrogen bond acceptor or donor, depending on its tautomeric state. It is preferably a hydrogen bond donor, but can tolerate being a hydrogen bond acceptor, as for example, when there is a methoxy at the R₄' position of the ligand;
- Arginines 228, 262, and 266 interact directly and through water-mediated hydrogen bonds with the R₁-substituent, with the electrostatic interaction provided by Arginine 266 (as in the Triac complex). This polar pocket is illustrated by FIG. 23 FIG. 25. FIG. 23 depicts T₃ in the TRI ligand binding cavity, where T3's amino-
- propionic R₁- substituent interacts with Arg 228, HOH502, H9H503 and HOH504 via hydrogen bonds. **FIG. 24** depicts Triac in the ligand binding cavity, with its -COOH R₁ substituent in the polar pocket. In **FIG. 24**, Arg 228 no longer shares a hydrogen bond with the ligand, but the -COOH R₁ substituent forms hydrogen bonds with Arg
- 20 266. FIG. 25 superimposes T₃ and Triac in the ligand binding cavity and shows several positionally unchanged amino acids and water molecules, and selected changed interacting amino acids and water molecules. The three figures illustrate parts of the polar pocket that can change and those parts that do not move upon binding of different ligands. For example, the Arg 262 at the top of the polar pocket
- 25 does not move, even when the R₁ substituent has changed from a -COOH to an aminopropionic acid group. However, the other two Arginines, Arg 228 and Arg 266, demonstrate flexibility in the polar pocket to respond to the change in the size or chemical naure of the R₁ substituent.
- 3) Inner and outer pockets for the R₃/R₅ substituents are formed by 30 Ser260, Ala263, Ile299; and Phe 218, Ile221, Ile222, respectively. See FIGS. 21 and 22. The inner pocket is filled by either the R₃ or the R₅ substituent, regardless of the size of the substituent, and may act as a binding determinant by positioning the ligand in the receptor. Optimally, the inner pocket amino acids interact with an R₃ or R₅

substituent, then the outer pocket interacts with the R₅ substituent and vice versa. The outer pocket can adjust to the size of its substituent through main chain motion centered at the break in helix 3 (Lys220-Ile221), suggesting that the bending of H3, and motion of the N-terminal portion of H3, may represent a conformational change induced on ligand binding. The outer pocket has greater flexibility than does the inner pocket in terms of accommodating a larger substituent group.

4) A pocket for the R₃'-substituent is formed by Phe 215, Gly290, Met388. The pocket is incompletely filled by the R₃'-iodo substituent, and 10 accommodates the slightly larger 3'-isopropyl substituent by movement of the flexible Met388 side chain and the H7/H8 loop. This pocket can accommodate R₃' substituents that are even larger than isopropyl, for example, a phenyl group.

The above information will facilitate the design of high affinity agonists and antagonists by improving automated QSAR methodologies and informing manual modeling of pharmaceutical lead compounds. For example, the inclusion of discrete water molecules provides a complete description of hydrogen bonding in the polar pocket for use with pharmacophore development: also, the identification of mobile and immobile residues within the receptor suggests physically reasonable constraints for use in molecular mechanics/dynamics calculations.

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Example 12. Design of an Increased Affinity Ligand

Direct interaction between the receptor and the ligand is limited in the polar pocket, which interacts with the R₁ substituent. While the lack of complementarity may contain implications for biological regulation, it also provides an opportunity for increasing affinity by optimizing the interaction between the amino acids of the polar pocket and the R₁ substituent of a synthetic ligand. The structure of the receptor-ligand interactions described herein enables design of an increased affinity synthetic ligand having two complementary modifications:

1) Remove the positively charged amine. The strongly positive 30 electrostatic potential predicted for the polar pocket suggests that the positively charged amine of the aminopropionic acid R₁ substituent may be detrimental to binding. Suitable groups for substitution are suggested by the nature of nearby hydrogen bond partners: for example, Thr 275 O or Ser 277 N. See e.g. Tables in Appendix 2. For example, any any negatively charged substituent would be

compatible for interacting with the amino acids of the polar pocket, including carboxylates, carbonyl, phosphonates, and sulfates, comprising 0 to 4 carbons. Another example of an R₁ substitution is an oxamic acid that replaces the amine of the naturally occurring ligand with one or more carbonyl groups.

5 Incorporate hydrogen bond acceptor and donor groups into the R₁substituent to provide broader interactions with the polar pocket scaffold. Such hydrogen bond acceptor and donor groups incorporated into the R1-substituent will allow interactions that would otherwise occur with water molecules in the polar pocket. Specific waters include HOH 504 (hydrogen bonds with Ala 225 O and Arg 10 262 NH); and HOH 503 hydrogen bonds with Asn 179 OD1, Ala 180 N), both of which are present in all four complexes (TR LBD complexed with T3, TR LBD complexed with IpBr2, TR LBD complexed with Dimit and TR LBD complexed with Triac). Analysis of the hydrogen bonding network in the polar pocket suggests replacement of HOH 504 with a hydrogen bond acceptor, and HOH 503 with an 15 hydrogen bond donor (although the chemical nature of asparagine probably permits flexibility at this site). Thus, incorporating a hydrogen bond acceptor in an R1 substituent that could take the place of the HOH504 or incorporating a hydrogen bond acceptor in an R1 substituent that could positionally replace the HOH503, or a combination thereof, are methods of designing novel synthetic TR ligands.

These two design approaches can be used separately or in combination to design synthetic ligands, including those in Table 5 (below).

A corollary to this approach is to design specific interactions to the residues Arg262 and Asn 179. The goal is to build in interactions to these residues by designing ligands that have R₁ substituents that form hydrogen bonds with water 25 molecules or charged residues in the polar pocket.

High-affinity ligands also may be designed and selected using small molecules that bind to proximal subsites of the target nuclear hormone receptor that are identified in a structure-based screen and then linked together in their experimentally determined bound orientiations. Such a method has been described in design of high-affinity ligands for the FK506 binding protein (FKBP), stromelysin, gelatinase A, and human papillomavirus E2 (Hajduk et al., Science 278:497-499 (1997)), which reference and its references are incorporated herein by reference. The preferred small molecules for screening are compounds of Formula I or derivatives thereof. For

example, a compound of Formula I (φ-X-φ) or a derivative thereof (φ-X or X-φ) is screened for binding a target nuclear hormone receptor LBD. Proximal subsites of the nuclear hormone receptor include the hydrophobic and polar pockets of the LBD, and substites extended therefrom. As an example, Fourier transformation or nuclear 5 magnetic resonance (NMR) -based structure screens can be used. When a NMR-based screen is used, binding can be detected from the amide chemical shift changes observed in two-dimensional heteronuclear single quantum correlation (HSQC) spectra aquired in the presence and absence of added compound. Once two ligands are identified that bind to the receptor, the crystal or solution structure of the ternary 10 complex is determined. From the structural information, a compound is synthesized which links the two ligands, where the linker is selected based on structural information. The new compound is then screened for binding affinity, for example, using a binding assay as described herein. Only a few linked ligands need to synthesized and screened when using this approach.

15 Compounds of the invention also may be interatively designed from structural information of the compounds described above using other structure-based design/modeling techniques (Jackson, R.C., Contributions of protein structure-based drug design to cancer chemotherapy. Semninars in Oncology, 1997, 24(2)L164-172; and Jones, T.R., et al., J. Med. Chem., 1996 39(4):904-917).

Table 5: Synthetic TR Ligands

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R1	R2	R3	R5	R6	X	R'2	R'3	R'4	R'5	R'6
СО2Н	Н	Me _.	Ме	Н	0	Н	Me	ОН	Me	Н
СН2СО2Н		1	1		S		Et	SH	Et	
CH2CH2CO2H		Br	Br				nPr	NH2	nPr	
CH2CH(NH2)CO2H		CI	CI				iPr		iPr	
ОСН2СО2Н		Et	Et				Ph		nBu	
осн2сн2со2н		ОН-	ОН				I		nPen	
NHCH2CO2H		NH2	NH2				Br	·	nHex	
NHCH2CH2CO2H		SH	SH				CI		Ph	
CH2COCOCO2H									hetero	
			•						cycle	
NHCOCOCO2H									aryl	
СОСО2Н										
CF2CO2H										
COCH2CO2H										

Any combination of the above substituents in the biphenyl ether scaffold structure shown above may result in a potentially pharmacologically useful ligand for the 10 thyroid hormone receptor. These novel ligands may be antagonists of the thyroid receptor.

TABLE 6: TR-α LBD-122/410

	Dimit .	Т3	IpBr₂	Triac
Data collection	•		, .	
Cell dimensions				
a (Å)	117.16	117.19	117.18	118.19
ь (Å)	80.52	80.20	80.12	81.37
c (Å)	63.21	63.23	63.13	63.73
β (°)	120.58	120.60	120.69	121.00
Resolution (Å)	2.2	2.0	2.1	2.45
Obs. Reflections, (no.)	57031	64424	66877	83573
Unique Reflections, (no.)	22327	21023	23966	18453
Completeness, (%)	87.0	82.4	93.7	96.0
*R _{sym} (%)	3.9	3.5	4.5	7.5
Phasing (15.0 - 2.5Å)				
†R _{der} (%)	•	19.6	11.6	
No. of sites	-	3	2	
‡Occupancy	-	44.6 (19.8)	35.0	
(Anomalous)	-	50.2 (23.7)	35.0	
		39.2 (22.3)		
§F _H /E				
centric (acentric)		•		
15.0-5.0 Å	-	3.67 (4.61)	2.25 (3.09)	
5.0-3.0 Å	-	2.23 (2.75)	1.25 (1.85)	
3.0-2.5 Å	-	1.64 (1.99)	1.15 (1.57)	
¶R _{Cullis} (%)				
15.0-5.0 Å	-	33	44	•
5.0-3.0 Å	•	45	63	
3.0-2.5 Å		60	65	
Mean figure of merit	0.62	-	-	
MR Phasing (10-3.5Å)				
Rotation Search:	-			$\Theta_1 = 309.37$
Euler Angles (°)				$\Theta_2 = 48.96$
			·	$\Theta_3 = 127.28$
§ correlation coefficient	•			34.3
Translation Search: Fractional coordinates		•		x = 0.1571
				y = 0.000
	,			z = 0.3421
§ correlation Coefficient				65.8
'R factor				31.2

Refinement Resolution (Å)	15.0-2.2	5.0 - 2.0	15.0 - 2.2	25-2 _. 5
¶R _{cryst (%)}	20.5	22.1	21.4	23.6
R _{free (%)}	22.7	24.0	22.4	24.1

TABLE 7: TR-β LBD-202/461

	Triac	T3	GC1
Data collection			
Space Group	- -	P3121	
Cell dimensions			
a (A)	68.9	68.45	68.73
c (Å)	131.5	130.56	130.09
Resolution (Å)	2.4	3.1	2.8
Obs. Reflections. (no.)	80196	55103	54104
Unique Reflections. (no.)	14277	6847	8987
Coverage (%)	97.0	95.7	97.1
*R _{sym} (%)	5.1	4.6	5.5
MR Phasing (15.0 - 3.5A)			
Rotation Search	$\Theta_1 = 39.13$		
Euler Angles (°)	⊖ ₂ =68:00		
,	⊕₃=323.6		
§ correlation coefficient	21.6		
(Highest false peak)	(10.8)		
Translation Search	x=0.748		
Fractional Coordinates	y=0.158		
	z=0.167		
§ correlation coefficient	57.5		
(Highest false peak)	(38.7)		
	0.612		
*R factor	40.7	40.8	
Refinement			
Resolution (Å)	30-2.4		30-2.9
¶R _{cryst (%)}	25.3		27.3
R _{free (%)}	28.9		33.4

All publications and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference. The nuclear receptor ligands, particularly the TR ligands, of these

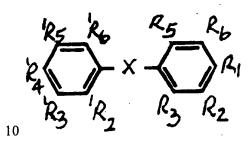
references are herein incorporated by reference and can be optionally excluded from the claimed compounds with a proviso.

Headings and subheadings are presented only for the convenience of the reader and should not be used to construe the meaning of terms used within such 5 headings and subheadings.

The invention now being fully described, it will be apparent to one of ordinary skill in the art that many changes and modifications can be made thereto without departing from the spirit or scope of the appended claims.

WHAT IS CLAIMED IS:

A method of modulating the activity of a thyroid hormone receptor
 (TR) which comprises administering to a mammal in need thereof a compound of the
 formula:



wherein said compound fits spatially and preferentially into a TR ligand binding domain (TR LBD) and comprises the following substituents:

- (i) an R₁-substituent comprising an anionic group that interacts with a side 15 chain nitrogen atom of an arginine corresponding to a residue selected from the group consisting of Arg228, Arg262, and Arg266 of human TR-α, and Arg282, Arg316 and Arg320 of human TR-β, and wherein the anionic group is 1.7-4.0Å from the nitrogen atom;
- (ii) an R₂-substituent comprising a hydrophobic or hydrophilic group that
 20 fits spacially into the TR LBD;
- (iii) an R₃-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a serine, alanine or isoleucine corresponding to a residue selected from the group consisting of Ser260, Ala263 and Ile299 of human TR-α, and Ser314, Ala317 and Ile352 of human TR-β, and wherein the hydrophobic or hydrophilic group is 1.7-4.0Å from the side chain atom;

(iv) an R₅-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a phenylalanine or isoleucine corresponding to a residue selected from the group consisiting of Phe218, Ile221 and Ile222 of human TR-I, and Phe272, Ile275 and Ile276 of human TR-β, and wherein the hydrophobic or hydrophilic group is 1.7-4.0Å from the side chain atom;

- (v) an R_6 -substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- (vi) an X-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a leucine corresponding to a residue selected from the group consisting of Leu276 and Leu292 of human TR-α, and Leu 330 and Leu346 of human TR-β, and wherein the hydrophobic or hydrophilic group is 1.7-4.0Å from the side chain atom;
 - (vii) an R₂'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- 15 (viii) an R₃'-substituent comprising a hydrophobic group that interacts with a side chain atom of a phenylalamine, glycine or methionine corresponding to a residue selected from the group consisting of Phe215, Gly290, and Met388 of human TR-α, and Phe269, Gly344, Met442 of human TR-β, and wherein the hydrophobic group is 1.7-4.0Å from the side chain atom;
- 20 (ix) an R₄'-substituent comprising an hydrogen bond donor or acceptor group that interacts with a side chain carbon or nitrogen atom of a histadine corresponding to residue His381 of human TR-α, and His435 of human TR-β, and wherein the hydrogen bond donor or acceptor group is 1.7-4.0Å from the side chain atom;

(x) an R₅'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;

- (xi) and R₆'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- wherein said compound is other than a thyronine or thyronine-like compound disclosed in a reference cited in Appendix I, and wherein the activity of said TR is modulated.
 - 2. The method according to claim 1,

10 wherein R₁ is

-O-CH₂CO₂H, -NHCH₂CO₂H,

-CO₂H, -CH₂CO₂H, -CH₂CH₂CO₂H, -CH₂CH₂CH₂CO₂H,

-CH₂CH(NH₂)CO₂H,

-CH₂CH[NHCOCH ϕ_2]CO₂H,

-CH₂CH[NHCO(CH₂)₁₅CH₃

]CO₂H,

-CH₂CH[NH-FMOC]CO₂H,

-CH₂CH[NH-tBOC]CO₂H, or a carboxylate connected to the ring with a 0 to 3 carbon linker,

 $-PO_3H_2$, $-CH_2PO_3H_2$, $-CH_2CH_2PO_3H_2$, $-CH_2CHNH_2PO_3H_2$,

 $-CH_2CH[NHCOCH\phi_2]PO_3H_2, \qquad -CH_2CH[NHCO(CH_2)_{15}CH_3]PO_3H_2,$

-CH₂CH[NH-FMOC]PO₃H₂, -CH₂ CH[NH-tBOC]PO₃H₂, or a phosphate or phosphonate connected to the ring with a 0 to 3 carbon linker,

-SO₃H, -CH₂SO₃H, -CH₂CH₂SO₃H, -CH₂CHNH₂SO₃H, -CH₂CH[NHCO(CH₂)₁₅CH₃]SO₃H,

-CH₂CH[NH-FMOC]SO₃H, -CH₂ CH[NH-tBOC]SO₃H, or a sulfate or sulfite connected to the ring with a 0 to 3 carbon linker,

or acts as the functional equivalent of CH₂CH(NH₂)CO₂H of T3 in the molecular recognition domain when bound to a TR, wherein said R₁ can be optionally substituted with an amine,

wherein R2 is

5

H, halogen, CF₃, OH, NH₂, SH, CH₃, -Et,

or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

wherein R₃ is

-H, halogen, -CF₃, -OH, -NH₂, -N₃, -SH, -CH₃, -Et,

or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR,

wherein R5 is

-H, halogen, -CF₃, -OH, -NH₂, -N₃, -SH, -CH₃, -Et, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR, and R₃ can be identical to R₅,

wherein R₆ is

-H, halogen, -CF₃, -OH, -NH₂, -SH, -CH₃, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR, and R₂ can be identical to R₆,

5 wherein R₂' is

-H, halogen, -CF₃, -OH, -NH₂, -N₃, -SH, -CH₃, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

wherein R₃' is any hydrophobic group, including

halogen, -CF₃, -SH, alkyl, aryl, 5- or 6-membered heterocyclie, cyano, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR,

wherein R4' is

-H, halogen, -CF₃, -OH, -NH₂, NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate or sulfate, -SH, -CH₃, -Et, or akyl, aryl or 5- or 6-membered heterocyclic aromatic attached through urea or carbamate linkages to O or N or S at the R₄' position, or acts as the functional equivalent of OH in the molecular recognition domain when bound to a TR,

20

25

wherein R₅' is

-H, -OH, -NH₂, -N(CH₃)₂ -SH -NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate. sulfate, branched or straight chain alkyl having 1 to 9 carbons, substituted or unsubstituted aryl, wherein said substituted aryl is substituted with halogen or 1 to 5 carbon alkyl and wherein said aryl is optionally

connected to the ring by a -CH₂-, aromatic heterocycle having 5 to 6 atoms, wherein said heterocycle may be substituted with one or more groups selected from -OH, -NH₂, -SH, -NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate or sulfate, heteroalkyl, arylalkyl, heteroaryl alkyl, polyaromatic, or polyheteroaromatic, wherein said R₅' may be substituted with polar or charged groups,

wherein R₆' is

-H, halogen, -CF₃, -OH, -NH₂, -SH, -CH₃, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

wherein X is

O, S, SO₂, NH, NR₇, CH₂, CHR₇, CR₇R₇, wherein R₇ is alkyl, aryl or 5- or 6-membered heterocyclic aromatic,

15

5

and wherein said TR LBD ligand has an apparent Kd for binding TR LBD of 1 TM or less.

- 3. The method of claim 2, wherein
- 20 R₁ is carboxylate, phosphonate, phosphate or sulfite and is connected to the ring with a 0 to 3 carbon linker,

R₂ is H,

R₃ is -I, -Br, or -CH₃,

 R_5 is -I, -Br, or -CH₃,

25 R₆ is H,

R₂' is H,

R₃' is -I, -Br, -CH₃, -iPr, -phenyl, benzyl, or 5- or 6-membered ring heterocycles,

R₄' is -OH, -NH₂, and -SH,

- phosphonate, phosphate, sulfate, branched or straight chain alkyl having 1 to 9 carbons, substituted or unsubstituted aryl, wherein said substituted aryl is substituted with halogen or 1 to 5 carbon alkyl and wherein said aryl is optionally connected to the ring by a -CH₂-, aromatic heterocycle having 5 to 6 atoms, wherein said heterocycle may be substituted with one or more groups selected from -OH, -NH₂, -SH, -NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate or sulfate, heteroalkyl, arylalkyl, heteroaryl alkyl, polyaromatic, or polyheteroaromatic, wherein said R₅' may be substituted with polar or charged groups, and
- 15 R₆' is H.
 - 4. The method of claim 1, wherein said compound fits spatially and preferentially into TR LBD isoform α (TR- α).
- 5. The method of claim 4, wherein said compound comprises an anionic group that interacts with the side chain oxygen or carbon of a serine residue corresponding to Ser277 of human TR-α, and wherein the anionic group is 1.7-4.0Å from the side chain atom.

6. The method of claim 1, wherein said compound fits spatially and preferentially into TR LBD isoform β (TR- β).

- The method of claim 6, wherein said compound comprises an anionic
 group that interacts with the side chain nitrogen of an arginine corresponding to
 Asn331 of human TR-β, and the anionic group is 1.7-4.0Å from the side chain atom.
- 8. A method for identifying a compound capable of selectively modulating the activity of a thyroid hormone receptor (TR) isoform, said method 10 comprising:

modeling test compounds that fit spacially and preferentially into a TR ligand binding domain (TR LBD) isoform of interest using an atomic structural model of a TR LBD isoform bound to a test compound,

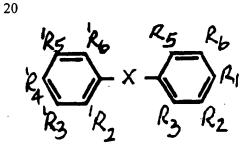
screening said test compounds in a biological assay for TR isoform

15 activity characterized by binding of a test compound to a TR LBD isoform, and

identifying a test compound that selectively modulates the activity of a

TR isoform.

9. The method of claim 8, wherein said compound is of the formula:



25

which comprises the following substituents:

- (i) an R₁-substituent comprising an anionic group that interacts with a side chain nitrogen atom of an arginine corresponding to a residue selected from the group consisting of Arg228, Arg262, and Arg266 of human TR-α, and Arg282, Arg316 and 5 Arg320 of human TR-β, and wherein the anionic group is 1.7-4.0Å from the nitrogen atom;
 - (ii) an R₂-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- (iii) an R₃-substituent comprising a hydrophobic or hydrophilic group that 10 interacts with a side chain atom of a serine, alanine or isoleucine corresponding to a residue selected from the group consisting of Ser260, Ala263 and Ile299 of human TR-α, and Ser314, Ala317 and Ile352 of human TR-β, and wherein the hydrophobic or hydrophilic group is 1.7-4.0Å from the side chain atom;
- (iv) an R₅-substituent comprising a hydrophobic or hydrophilic group that 15 interacts with a side chain atom of a phenylalanine or isoleucine corresponding to a residue selected from the group consisiting of Phe218, Ile221 and Ile222 of human TR-α, and Phe272, Ile275 and Ile276 of human TR-β, and wherein the hydrophobic or hydrophilic group is 1.7-4.0Å from the side chain atom;
- (v) an R₆-substituent comprising a hydrophobic or hydrophilic group that
 20 fits spacially into the TR LBD;
- (vi) an X-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a leucine corresponding to a residue selected from the group consisting of Leu276 and Leu292 of human TR-α, and Leu 330 and Leu346 of human TR-β, and wherein the hydrophobic or hydrophilic group is 1.7-4.0Å from 25 the side chain atom;

(vii) an R₂'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;

- (viii) an R₃'-substituent comprising a hydrophobic group that interacts with a side chain atom of a phenylalamine, glycine or methionine corresponding to a residue selected from the group consisting of Phe215, Gly290, and Met388 of human TR-α, and Phe269. Gly344, Met442 of human TR-β, and wherein the hydrophobic group is 1.7-4.0Å from the side chain atom;
- (ix) an R₄'-substituent comprising an hydrogen bond donor or acceptor group that interacts with a side chain carbon or nitrogen atom of a histadine 10 corresponding to residue His381 of human TR-α, and His435 of human TR-β, and wherein the hydrogen bond donor or acceptor group is 1.7-4.0Å from the side chain atom;
 - (x) an R₅'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD; and
- 15 (xi) and R₆'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD.
 - 10. The method according to claim 9, wherein R_1 is
- $-O-CH_2CO_2H$, $-NHCH_2CO_2H$,
 - -CO₂H₁, -CH₂CO₂H₁, -CH₂CH₂CO₂H₂, -CH₂CH₂CO₂H₃,
 - -CH₂CH(NH₂)CO₂H,

-CH₂CH[NHCOCH ϕ_2]CO₂H,

- -CH2CH[NHCO(CH2)15CH3
- CO_2H ,
- -CH₂CH[NH-FMOC]CO₂H,
- -CH₂CH[NH-tBOC]CO₂H, or a carboxylate connected to the ring with a 0 to 3
- 25 carbon linker,

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-PO₃H₂, -CH₂PO₃H₂, -CH₂CH₂PO₃H₂, -CH₂CHNH₂PO₃H₂,
-CH₂CH[NHCOCHφ₂]PO₃H₂, -CH₂CH[NHCO(CH₂)₁₅CH₃]PO₃H₂,
-CH₂CH[NH-FMOC]PO₃H₂, -CH₂ CH[NH-tBOC]PO₃H₂, or a phosphate or phosphonate connected to the ring with a 0 to 3 carbon linker,

-SO₃H, -CH₂SO₃H, -CH₂CH₂SO₃H, -CH₂CHNH₂SO₃H,
-CH₂CH[NHCOCHφ₂]SO₃H, -CH₂CH[NHCO(CH₂)₁₅CH₃]SO₃H,
-CH₂CH[NH-FMOC]SO₃H, -CH₂ CH[NH-tBOC]SO₃H, or a sulfate or sulfite connected to the ring with a 0 to 3 carbon linker,

or acts as the functional equivalent of $CH_2CH(NH_2)CO_2H$ of T3 in the molecular recognition domain when bound to a TR, wherein said R_1 can be optionally substituted with an amine,

15

10

wherein R2 is

H, halogen, CF₃, OH, NH₂, SH, CH₃, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

20

wherein R₃ is

-H, halogen, -CF₃, -OH, -NH₂, -N₃, -SH, -CH₃, -Et, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR,

25

wherein R5 is

-H, halogen, -CF₃, -OH, -NH₂, -N₃, -SH, -CH₃, -Et, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR, and R_3 can be identical to R_5 ,

5

wherein R₆ is

-H, halogen, -CF₃, -OH, -NH₂, -SH, -CH₃, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR, and R₂ can be identical to R₆,

10

wherein R2' is

-H, halogen, -CF₃, -OH, -NH₂, -N₃, -SH, -CH₃, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

15 wherein R₃' is any hydrophobic group, including

halogen, -CF₃, -SH, alkyl, aryl, 5- or 6-membered heterocyclie, cyano, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR,

20 wherein R₄' is

25

-H, halogen, -CF₃, -OH, -NH₂, NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate or sulfate, -SH, -CH₃, -Et, or akyl, aryl or 5- or 6-membered heterocyclic aromatic attached through urea or carbamate linkages to O or N or S at the R₄' position, or acts as the functional equivalent of OH in the molecular recognition domain when bound to a TR,

wherein R5' is

5

10

-H, -OH, -NH₂, -N(CH₃)₂ -SH -NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate, sulfate, branched or straight chain alkyl having 1 to 9 carbons, substituted or unsubstituted aryl, wherein said substituted aryl is substituted with halogen or 1 to 5 carbon alkyl and wherein said aryl is optionally connected to the ring by a -CH₂-, aromatic heterocycle having 5 to 6 atoms, wherein said heterocycle may be substituted with one or more groups selected from -OH, -NH₂, -SH, -NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate or sulfate, heteroalkyl, arylalkyl, heteroaryl alkyl, polyaromatic, or polyheteroaromatic, wherein said R₅' may be substituted with polar or charged groups,

wherein R₆' is

-H, halogen, -CF₃, -OH, -NH₂, -SH, -CH₃, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

wherein X is

O, S, SO₂, NH, NR₇, CH₂, CHR₇, CR₇R₇, wherein R₇ is alkyl, aryl or 5- or 6-membered heterocyclic aromatic,

and wherein said TR LBD ligand has an apparent Kd for binding TR LBD of 1 TM or less.

25 11. The method of claim 10, wherein

5

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 R_1 is carboxylate, phosphonate, phosphate or sulfite and is connected to the ring with a 0 to 3 carbon linker,

R₂ is H,

R₃ is -I, -Br, or -CH₃,

 R_5 is -I, -Br, or -CH₃,

R₆ is H,

R₂' is H,

R₃' is -I, -Br, -CH₃, -iPr, -phenyl, benzyl, or 5- or 6-membered ring heterocycles,

10 R_4 ' is -OH, -NH₂, and -SH,

R₅' is -H, -OH, -NH₂, -N(CH₃)₂ -SH -NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate, sulfate, branched or straight chain alkyl having 1 to 9 carbons, substituted or unsubstituted aryl, wherein said substituted aryl is substituted with halogen or 1 to 5 carbon alkyl and wherein said aryl is optionally connected to the ring by a -CH₂-, aromatic heterocycle having 5 to 6 atoms, wherein said heterocycle may be substituted with one or more groups selected from -OH, -NH₂, -SH, -NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate or sulfate, heteroalkyl, arylalkyl, heteroaryl alkyl, polyaromatic, or polyheteroaromatic, wherein said R₅' may be substituted with polar or charged groups, and

. R₆' is H.

12. The method of claim 8, wherein said compound fits spatially and preferentially into TR LBD isoform α (TR- α).

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13. The method of claim 12, wherein said compound comprises an anionic group that interacts with the side chain oxygen or carbon of a serine residue corresponding to Ser277 of human TR-α, and wherein the anionic group is 1.7-4.0Å from the side chain atom.

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- 14. The method of claim 8, wherein said compound fits spatially and preferentially into TR LBD isoform β (TR- β).
- 15. The method of claim 14, wherein said compound comprises an anionic 10 group that interacts with the side chain nitrogen of an arginine corresponding to Asn331 of human TR-β, and the anionic group is 1.7-4.0Å from the side chain atom.
 - 16. The method of claim 8, wherein said compound binds to a TR LBD isoform with greater affinity than thyronine or triidothyronine.

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- 17. A method for identifying a thyroid hormone receptor (TR) agonist or antagonist ligand, said method comprising the steps of:
- providing the atomic coordinates of a TR ligand binding domain (TR LBD) to a computerized modeling system;
- 20 modeling ligands which fit spacially into the TR LBD; and

identifying in a biological assay for TR activity a ligand which increases or descreases the activity of said TR, whereby a TR agonist or antagonist is identified.

18. A peptide, peptidomimetic or synthetic molecule identified by the method of any one of claims 8 or 17, with the proviso that said molecule is other than a thyronine or thyronine-like compound disclosed in a reference cited in Appendix I.

5 19. A method of identifying a compound that selectively modulates the activity of a thyroid hormone receptor (TR) compared to other nuclear hormone receptors, said method comprising:

modeling compounds which fit spacially into a TR ligand binding domain (TR LBD) using an atomic structural model of a TR LBD,

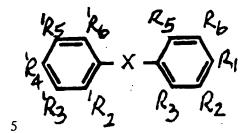
selecting a compound comprising conformationally constrained structural features that interact with conformationally constrained residues of a TR LBD,

identifying in a biological assay for TR activity a compound that selectively binds to a TR LBD compared to other nuclear receptors, whereby a 15 compound that selectively modulates a TR is identified.

- 20. The method of claim 19, wherein said conformationally constrained residues of a TR LBD correspond to residues Met259, Leu276, Leu292, His381, Gly290, Ile221, and Phe401 of human TR-α, and residues Met313, Leu330, Leu346, 20 His435, Gly344, Ile275 and Phe455 of human TR-β.
 - 21. The method of claim 19, wherein said compounds are of the formula:

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which comprises the following substituents:

- (i) an R₁-substituent comprising an anionic group that interacts with a side chain nitrogen atom of an arginine corresponding to a residue selected from the group 10 consisting of Arg228, Arg262, and Arg266 of human TR-α, and Arg282, Arg316 and Arg320 of human TR-β, and wherein the anionic group is 1.7-4.0Å from the nitrogen atom;
 - (ii) an R₂-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- 15 (iii) an R₃-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a serine, alanine or isoleucine corresponding to a residue selected from the group consisting of Ser260, Ala263 and Ile299 of human TR-α, and Ser314, Ala317 and Ile352 of human TR-β, and wherein the hydrophobic or hydrophilic group is 1.7-4.0Å from the side chain atom;
- 20 (iv) an R₅-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a phenylalanine or isoleucine corresponding to a residue selected from the group consisting of Phe218, Ile221 and Ile222 of human TR-α, and Phe272, Ile275 and Ile276 of human TR-β, and wherein the hydrophobic or hydrophilic group is 1.7-4.0Å from the side chain atom;

(v) an R₆-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;

- (vi) an X-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a leucine corresponding to a residue selected from 5 the group consisting of Leu276 and Leu292 of human TR-α, and Leu 330 and Leu346 of human TR-β, and wherein the hydrophobic or hydrophilic group is 1.7-4.0Å from the side chain atom;
 - (vii) an R₂'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- 10 (viii) an R₃'-substituent comprising a hydrophobic group that interacts with a side chain atom of a phenylalanine, glycine or methionine corresponding to a residue selected from the group consisting of Phe215, Gly290, and Met388 of human TR-α, and Phe269, Gly344, Met442 of human TR-β, and wherein the hydrophobic group is 1.7-4.0Å from the side chain atom;
- 15 (ix) an R₄'-substituent comprising an hydrogen bond donor or acceptor group that interacts with a side chain carbon or nitrogen atom of a histidine corresponding to residue His381 of human TR-α, and His435 of human TR-β, and wherein the hydrogen bond donor or acceptor group is 1.7-4.0Å from the side chain atom;
- 20 (x) an R₅'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD; and
 - (xi) and R₆'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD.
- 25 22. The method of claim 19, wherein said compound comprises:

- (i) a cyclic carbon atom that interacts with a carbon and oxygen atom of a methionine residue corresponding to Met259 of human TR-α, and Met313 of human TR-β, wherein the cyclic carbon is about 3.0 to 4.0Å from the carbon and oxygen atom of the methionine;
- 5 (ii) a cyclic carbon atom that interacts with a carbon atom of a leucine residue corresponding to Leu276 of human TR-α, and Leu330 of human TR-β, wherein the cyclic carbon is about 3.0 to 4.0Å from the carbon atom of the leucine;
- (iii) a cyclic carbon atom that interacts with a carbon atom of a leucine residue corresponding to Leu292 of human TR-α, and Leu346 of human TR-β,
 10 wherein the cyclic carbon is about 3.0 to 4.0Å from the carbon atom of the leucine;
 - (iv) a R₃-substituent comprising an atom that interacts with a carbon atom of an isoleucine residue corresponding to Ile221 of human TR-α, and Ile275 of human TR-β, wherein the R3-substituent atom is about 3.0 to 4.0Å from the carbon atom of the isoleucine;
- 15 (v) a R₃'-substituent comprising an atom that interacts with an oxygen atom of a glycine residue corresponding to Gly290 of human TR-α, and Gly344 of human TR-β, wherein the R3'-substituent atom is about 3.0 to 4.0Å from the carbon atom of the glycine; and
- (vi) a R₄'-substituent comprising an atom selected from the group 20 consisting of oxygen and carbon that interacts with (a) a carbon and nitrogen atom of a histidine residue corresponding to His381 of human TR-α, and His435 of human TR-β, wherein the R4'-substituent atom is about 2.0 to 4.0Å from the carbon atom of the histidine; and (b) a carbon atom of a phenylalanine residue corresponding to Phe401 of human TR-α, and human Phe455 of TR-β, wherein said atom is about 3.0 to 4.0Å from the carbon atom of the phenylalanine.

23. The method according to claim 21,

wherein R₁ is

-O-CH₂CO₂H, -NHCH₂CO₂H,

5 -CO₂H, -CH₂CO₂H, -CH₂CH₂CO₂H, -CH₂CH₂CO₂H,

-CH₂CH(NH₂)CO₂H,

-CH₂CH[NHCOCHφ₂]CO₂H,

-CH2CH[NHCO(CH2)15CH3

]CO₂H,

-CH₂CH[NH-FMOC]CO₂H,

-CH₂CH[NH-tBOC]CO₂H, or a carboxylate connected to the ring with a 0 to 3 carbon linker,

10

 $-PO_3H_2, \qquad -CH_2PO_3H_2, \qquad -CH_2CH_2PO_3H_2, \qquad -CH_2CHNH_2PO_3H_2,$

-CH₂CH[NHCOCH ϕ_2]PO₃H₂,

-CH₂CH[NHCO(CH₂)₁₅CH₃]PO₃H₂,

-CH₂CH[NH-FMOC]PO₃H₂, -CH₂ CH[NH-tBOC]PO₃H₂, or a phosphate or

phosphonate connected to the ring with a 0 to 3 carbon linker,

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 $-SO_3H$, $-CH_2SO_3H$,

-CH₂CH₂SO₃H,

-CH₂CHNH₂SO₃H,

-CH₂CH[NHCOCH ϕ_2]SO₃H,

-CH₂CH[NHCO(CH₂)₁₅CH₃]SO₃H,

-CH2CH[NH-FMOC]SO3H, -CH2 CH[NH-tBOC]SO3H, or a sulfate or sulfite

connected to the ring with a 0 to 3 carbon linker,

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or acts as the functional equivalent of $CH_2CH(NH_2)CO_2H$ of T3 in the molecular recognition domain when bound to a TR, wherein said R_1 can be optionally substituted with an amine,

25 wherein R₂ is

H, halogen, CF₃, OH, NH₂, SH, CH₃, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

5 wherein R₃ is

-H, halogen, -CF₃, -OH, -NH₂, -N₃, -SH, -CH₃, -Et, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR,

10 wherein R₅ is

-H, halogen, -CF₃, -OH, -NH₂, -N₃, -SH, -CH₃, -Et, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR, and R_3 can be identical to R_5 ,

15 wherein R₆ is

-H, halogen, -CF₃, -OH, -NH₂, -SH, -CH₃, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR, and R₂ can be identical to R₆,

20 wherein R₂' is

-H, halogen, -CF₃, -OH, -NH₂, -N₃, -SH, -CH₃, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

wherein R₃' is any hydrophobic group, including

halogen, -CF₃, -SH, alkyl, aryl, 5- or 6-membered heterocycle, cyano, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR,

5 wherein R₄' is

-H, halogen, -CF₃, -OH, -NH₂, NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate or sulfate, -SH, -CH₃, -Et, or akyl, aryl or 5- or 6-membered heterocyclic aromatic attached through urea or carbamate linkages to O or N or S at the R₄' position, or acts as the functional equivalent of OH in the molecular recognition domain when bound to a TR,

wherein R5' is

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-H, -OH, -NH₂, -N(CH₃)₂ -SH -NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate, sulfate, branched or straight chain alkyl having 1 to 9 carbons, substituted or unsubstituted aryl, wherein said substituted aryl is substituted with halogen or 1 to 5 carbon alkyl and wherein said aryl is optionally connected to the ring by a -CH₂-, aromatic heterocycle having 5 to 6 atoms, wherein said heterocycle may be substituted with one or more groups selected from -OH, -NH₂, -SH, -NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate or sulfate, heteroalkyl, arylalkyl, heteroaryl alkyl, polyaromatic, or polyheteroaromatic, wherein said R₅' may be substituted with polar or charged groups,

wherein R₆' is

-H, halogen, -CF₃, -OH, -NH₂, -SH, -CH₃, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

wherein X is

O, S, SO₂, NH, NR₇, CH₂, CHR₇, CR₇R₇, wherein R₇ is alkyl, aryl or 5- or 6-membered heterocyclic aromatic,

and wherein said TR LBD ligand has an apparent Kd for binding TR LBD of 1 TM or less.

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24. The method of claim 23, wherein

R₁ is carboxylate, phosphonate, phosphate or sulfite and is connected to the ring with a 0 to 3 carbon linker,

R₂ is H,

15 R_3 is -I, -Br, or -CH₃,

R₅ is -I, -Br, or -CH₃,

R₆ is H,

R₂' is H,

R₃' is -I, -Br, -CH₃, -iPr, -phenyl, benzyl, or 5- or 6-membered ring

20 heterocycles,

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R₄' is -OH, -NH₂, and -SH,

R₅' is -H, -OH, -NH₂, -N(CH₃)₂ -SH -NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate, sulfate, branched or straight chain alkyl having 1 to 9 carbons, substituted or unsubstituted aryl, wherein said substituted aryl is substituted with halogen or 1 to 5 carbon alkyl and wherein said aryl is

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optionally connected to the ring by a -CH₂-, aromatic heterocycle having 5 to 6 atoms, wherein said heterocycle may be substituted with one or more groups selected from -OH, -NH₂, -SH, -NH₃, -N(CH₃)₃, carboxylate, phosphonate, phosphate or sulfate, heteroalkyl, arylalkyl, heteroaryl alkyl, polyaromatic, or polyheteroaromatic, wherein said R₅' may be substituted with polar or charged groups, and

R₆' is H.

- 25. The method of claim 19, wherein said compound fits spatially and 10 preferentially into TR LBD isoform α (TR- α).
- 26. The method of claim 25, wherein said compound comprises an anionic group that interacts with the side chain oxygen or carbon of a serine residue corresponding to Ser277 of human TR-α, and wherein the anionic group is 1.7-4.0Å
 15 from the side chain atom.
 - 27. The method of claim 19, wherein said compound fits spatially and preferentially into TR LBD isoform β (TR- β).
- 28. The method of claim 27, wherein said compound comprises an anionic group that interacts with the side chain nitrogen of an arginine corresponding to Asn331 of human TR-β, and the anionic group is 1.7-4.0Å from the side chain atom.
- 29. The method of claim 19, wherein said compound binds to a TR LBD 25 isoform with greater affinity than thyronine or triiodothyronine.

30. The method of claim 1, wherein said compound comprises a cyclic carbon atom that interacts with a carbon and oxygen atom of a methionine residue corresponding to Met259 of human TR-I, and Met313 of human TR-β, wherein the cyclic carbon is about 3.0 to 4.0Å from the carbon and oxygen atom of the methionine.

31. The method of claim 30, wherein said cyclic carbon is inner ring carbon C11.

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32. The method of claim 1, wherein said compound comprises a cyclic carbon atom that interacts with a carbon atom of a leucine residue corresponding to Leu276 of human TR- α , and Leu330 of human TR- β , wherein the cyclic carbon is about 3.0 to 4.0Å from the carbon atom of the leucine.

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- 33. The method of claim 32, wherein said cyclic carbon is selected from the group consisting of inner ring carbons C7 and C9.
- 34. The method of claim 1, wherein said compound comprises a cyclic 20 carbon atom that interacts with a carbon atom of a leucine residue corresponding to Leu292 of human TR-α, and Leu346 of human TR-β, wherein the cyclic carbon is about 3.0 to 4.0Å from the carbon atom of the leucine.
- 35. The method of claim 34, wherein said cyclic carbon is selected from 25 the group consisting of outer ring carbons C6 and C8.

36. The method of claim 1, wherein said R₃-substituent comprises an atom that interacts with a carbon atom of an isoleucine residue corresponding to Ile221 of human TR-α, and Ile275 of human TR-β, wherein the R₃-substituent atom is about
5 3.0 to 4.0Å from the carbon atom of the isoleucine.

- 37. The method of claim 1, wherein said R₃'-substituent comprises an atom that interacts with an oxygen atom of a glycine residue corresponding to Gly290 of human TR-α, and Gly344 of human TR-β, wherein the R₃'-substituent atom is 10 about 3.0 to 4.0Å from the carbon atom of the glycine.
- 38. The method of claim 1, wherein said R₄'-substituent comprises an atom selected from the group consisting of oxygen and carbon that interacts with a carbon and nitrogen atom of a histidine residue corresponding to His381 of human 15 TR-α, and His435 of human TR-β, wherein the R₄'-substituent atom is about 2.0 to 4.0Å from the carbon atom of the histidine.
- 39. The method of claim 1, wherein said R₄'-substituent comprises an oxygen atom that interacts with a carbon atom of a phenylalanine residue
 20 corresponding to Phe401 of human TR-α, and human Phe455 of TR-β, wherein said atom is about 3.0 to 4.0Å from the carbon atom of the phenylalanine.
- 40. A method for identifying a thyroid hormone receptor (TR) agonist or antagonist ligand that selectively modulates the activity of a TR compared to other 25 nuclear receptors, said method comprising the steps of:

providing the atomic coordinates of a TR ligand binding domain (TR LBD) to a computerized modeling system;

modeling ligands which fit spacially into the TR LBD and which interact with conformationally constrained residues of a TR LBD conserved among 5 TR isoforms; and

identifying in a biological assay for TR activity a ligand which selectively binds to said TR and increases or decreases the activity of said TR, whereby a TR agonist or antagonist that selectively modulates the activity of a TR is identified.

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- 41. A peptide, peptidomatic or synthetic molecule identified by the method of any one of claims 19 or 40, with the proviso that said molecule is other than a thyronine or thyronine-like compound disclosed in a reference cited in Appendix I.
- 15 42. A machine-readable data storage medium, comprising a data storage material encoded with machine readable data which, when using a machine programmed with instructions for using said data, is capable of displaying a graphical three-dimensional representation of a molecule or molecular complex for a thyroid hormone ligand binding pocket comprising structure coordinates of TR-α amino acids 20 corresponding to human TR-α amino acids Met259, Leu276, and Ile221, or a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

43. A machine-readable data storage medium, comprising a data storage material encoded with machine readable data which, when using a machine programmed with instructions for using said data, is capable of displaying a graphical three-dimensional representation of a molecule or molecular complex for a thyroid 5 hormone ligand binding pocket comprising structure coordinates of TR-α amino acids corresponding to human TR-α amino acids Leu292, His381, Gly290 and Phe401, or a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

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44. The machine-readable storage medium according to any one of claims 42 or 43, wherein said binding pocket comprises structure coordinates of TR- α amino acids corresponding to human TR- α amino acids Met259, Leu276, Leu292, His381, Gly290, Ile221 and Phe401.

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- 45. The machine-readable storage medium according to claim 44, wherein said binding pocket comprises structure coordinates of TR-α amino acids corresponding to human TR-α amino acids Arg228, Arg262 and Arg266.
- 20 46. The machine-readable storage medium according to claim 44, wherein said binding pocket comprises structure coordinates of TR-α amino acids corresponding to human TR-α amino acids Ser260, Ala263 and Ile299.

47. The machine-readable storage medium according to claim 44, wherein said binding pocket comprises structure coordinates of TR- α amino acids corresponding to human TR- α amino acids Phe218, Ile221 and Ile222.

- 5 48. The machine-readable storage medium according to claim 44, wherein said binding pocket comprises structure coordinates of TR-α amino acids corresponding to human TR-α amino acids Phe215, Gly290 and Met388.
- 49. The machine-readable storage medium according to claim 44, wherein 10 said binding pocket comprises structure coordinates of a TR-α amino acid corresponding to human TR-α amino acid Ser277.
- 50. A machine-readable data storage medium, comprising a data storage material encoded with machine readable data which, when using a machine programmed with instructions for using said data, is capable of displaying a graphical three-dimensional representation of a molecule or molecular complex for a thyroid hormone ligand binding pocket comprising structure coordinates of TR-β amino acids corresponding to human TR-β amino acids Met313, Leu330, and Ile275, or a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.
- 51. A machine-readable data storage medium, comprising a data storage material encoded with machine readable data which, when using a machine programmed with instructions for using said data, is capable of displaying a graphical

three-dimensional representation of a molecule or molecular complex for a thyroid hormone ligand binding pocket comprising structure coordinates of TR-β amino acids corresponding to human TR-β amino acids Leu346, His435, Gly344, and Phe455, or a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

- 52. The machine-readable data storage medium according to any one of claims 50 or 51, wherein said binding pocket comprises structure coordinates of TR-β
 10 amino acids corresponding to human TR-β amino acids Met313, Leu330, Leu346, His435, Gly344, Ile275 and Phe455.
- 53. The machine-readable data storage medium according to claim 52,
 wherein said binding pocket comprises structure coordinates of TR-β amino acids
 15 corresponding to human TR-β amino acids Arg282, Arg316 and Arg320.
 - 54. The machine-readable data storage medium according to claim 52, wherein said binding pocket comprises structure coordinates of TR-β amino acids corresponding to human TR-β amino acids Ser314, Ala317 and Ile352.

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55. The machine-readable data storage medium according to claim 52, wherein said binding pocket comprises structure coordinates of TR-β amino acids corresponding to human TR-β amino acids Phe272, Ile275 and Ile276.

56. The machine-readable data storage medium according to claim 52, wherein said binding pocket further comprises structure coordinates of TR-β amino acids corresponding to human TR-β amino acids Phe269, Gly344 and Met442.

- 5 57. The machine-readable data storage medium according to claim 52, wherein said binding pocket comprises structure coordinates of a TR-β amino acid corresponding to human TR-β amino acid Asn331.
- 58. The machine-readable data storage medium according to claim 52, 10 wherein said molecule or molecular complex is defined by the set of structure coordinates selected from the group consisting coordinates depicted in Appendix 3, 4, 5 and 6, or a homologue of said molecule or molecular complex, said homologue having a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

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- 59. The machine-readable data storage medium according to claim 52, wherein said molecule or molecular complex is defined by the set of structure coordinates selected from the group consisting coordinates depicted in Appendix 7 and 8, or a homologue of said molecule or molecular complex, said homologue 20 having a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.
- 60. A machine-readable data storage medium comprising a data storage material encoded with a first set of machine readable data which, when combined 25 with a second set of machine readable data, using a machine programmed with

instructions for using said first set of data and said second set of data, can determine at least a portion of the structure coordinates corresponding to the second set of machine readable data, wherein: said first set of data comprises a Fourier transform of at least a portion of the structural coordinates selected from the group consisting of coordinates depicted in Appendix 3, 4, 5, 6, 7 and 8; and said second set of data comprises an X-ray diffraction pattern of a molecule or molecular complex.

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APPENDIX 1

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APPENDIX 2

Table 8

Dimit	Amino Acid	Amino Acid	Distance
Atom	in full length α	Atom	Å
C16	215-PHE	CD1	3.98
C16	215-PHE	CE1	3.86
C19	218-PHE	0	3.69
C16	218-PHE	СВ	3.89
C18	218-PHE	СВ	3.92
C19	218-PHE	СВ	4.13
C18	218-PHE	CD2	3.77
C16	219-THR	CG2	3.68
C19	221-ILE	CG1	4.11
C6	222-ILE	CD1	4.18
C8	222-ILE	CD1	3.72
C10	222-ILE	CD1	3.53
C12	222-ILE	CD1	3.85
O1	222-ILE	CD1	4.13
C13	225-ALA	C8	3.64
04	225-ALA	C8	4.02
04	228-ARG	CZ	3.96
C17	228-ARG	NH2	3.36
O3	228-ARG	NH2	3.58
O4	228-ARG	NH2	2.86
C10	256-MET	SD	3.70
C12	256-MET	SD	3.89
C10	256-MET	CE	3.88
C12	256-MET	CE	3.83
C11	259-MET	С	4.03
C11	259-MET	0	3.66
C15	259-MET	0	3.42
N1	259-MET	0	3.71
Cl	259-MET	C8	4.20
C11	259-MET	C8	3.87
C13	259-MET	C8	4.09
C15	262-ARG	C8	4.03
C17	262-ARG	C8	3.58
O3	262-ARG	C8	3.62
04	262-ARG	C8	3.85
C17	262-ARG	CD	4.10
04	262-ARG	CD	3.61
NI	263-ALA	N	3.71
C17	263-ALA	CA	3.69
NI	263-ALA	СВ	3.46
O3	266-ARG	NHI	3.93

Dimit	Amino Acid	Amino Acid	<u>Distance</u>
Atom	in full length α	Atom	Å
N1	275-THR	0	3.62
NI	276-LEU	CA	3.51
N1	276-LEU	С	3.92
C5	276-LEU	CD1	4.05
C19	276-LEU	CD1	4.04
C7	276-LEU	CD2	4.09
С9	276-LEU	CD2	3.95
C11	276-LEU	CD2	4.13
NI	276-LEU	CD2	4.17
C13	277-SER	N	4.14
C15	277-SER	N	3.79
C17	277-SER	N	3.69
N1	277-SER	N	3.30
O3	277-SER	N	3.19
C17	277-SER	CA	3.92
O3	277-SER	CA	3.35
C13	277-SER	OG	3.92
C7	287-LEU	CD2	3.90
C18	290-GLY	С	4.04
C18	290-GLY	0	3.54
C18	291-GLY	CA	4.04
C18	292-LEU	N	4.20
C2	292-LEU	CG	4.18
C4	292-LEU	CG	3.86
C6	292-LEU	CG	4.01
C2	292-LEU	CD1	3.88
C4	292-LEU	CD1	4.02
O2	292-LEU	CD1	4.07
C4	292-LEU	CD2	4.05
C6	292-LEU	CD2	3.72
C8	292-LEU	CD2	3.69
C10	292-LEU	CD2	3.98
O1	292-LEU	CD2	4.16
C20	299-ILE	CD1	3.87
C8	381-HIS	CD2	3.90
C10	381-HIS	CD2	3.84
01	381-HIS	GO2	3.40
01	381-HIS	CE1	3.72
C8	381-HIS	NE2	3.47
C10	381-HIS	NE2	3.51
01	381-HIS	NE2	2.64
C6	388-MET	CE	3.90
C8	401-PHE	CE1	4.19
Ol	401-PHE	CE1	3.37

Dimit	Amino Acid	Amino Acid	<u>Distance</u>
Atom	in full length α	Atom	Å
C16	401-PHE	CZ	3.97
O1	401-PHE	CZ	3.28
N1	502-H ₂ O	01	3.35
O3	502-H ₂ O	01	2.56
O3	503-H ₂ O	Ol	3.13
O4	503-H ₂ O	01	3.72
04	504-H ₂ O	01	2.72

Legend to Table 8. The table lists the interactions with Dimit (DMT). The column headings are as follows:

- #1 The atom of Dimit that interacts with the amino acid of the receptor. These are also 5 numbered in Figure 32.
 - #2 The amino acid in the full length rTR α that interacts with the ligand.
 - #3 The name of the atom in the amino acid (standard nomenclature) where the interaction occurs.
 - #4 The distance in Å between Dimit and the protein atom.

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Table 9

Triac	Amino Acid	Amino Acid	
Atom	in full length α	Atom	Distance Å
II I	218-PHE	0	3.52
II II	221-ILE	CD1	4.16
I1	221-ILE	CG1	3.92
Il	222-ILE	CA	4.15
I1	222-ILE	СВ	4.03
Ĭ1	222-ILE	CG1	3.92
C8	222-ILE	CD1	4.12
C10	222-ILE	CD1	3.77
C12	222-ILE	CD1	3.79
C13	225-ALA	СВ	4.17
C3	225-ALA	СВ	3.86
C10	256-MET	SD	3.45
C12	256-MET	SD	3.73
C10	256-MET	CE	3.66
C12	256-MET	CE	3.77
I3	256-MET	CE	3.89
Cl	259-MET	0	3.93
C11	259-MET	0	3.24
O3	259-MET	0	4.09
C1	259-MET	СВ	3.89
C13	259-MET	0	3.74
C14	259-MET	0	3.96
Cl	259-MET	СВ	3.89
C11	259-MET	CB	3.68
C13	259-MET	CB	4.01
C11	259-MET	CA	4.13
C13	259-MET	CA	4.20
I3 ·	260-SER	CA	4.10
I3	260-SER	OG	4.19
C14	262-ARG	CB	4.07
04	262-ARG	СВ	3.60
O3	263-ALA	N	3.79
C14	263-ALA	N	4.12
O3	263-ALA	CA	3.67
O3	263-ALA	CB	3.49
C11	263-ALA	СВ	4.00
C14	266-ARG	CZ	3.89
03	266-ARG	CZ	4.01
04	266-ARG	CZ	3.03
C14	266-ARG	NH1	3.25
O3	266-ARG	NH1	3.00
04	266-ARG	NH1	2.82

Triac	Amino Acid	Amino Acid	
Atom	in full length α	Atom	Distance Å
C14	266-ARG	NH2	3.48
03	266-ARG	NH2	4.01
04	266-ARG	NH2	2.34
03	275-THR	С	4.02
C14	275-THR	0	4.20
O3	275-THR	0	3.20
O3	278-LEU	CA	3.11
03	276-LEU	С	3.52
. O3	276-LEU	N	4.04
C14	276-LEU	CA	3.98
O3	276-LEU	CA	3.11
C14	276-LEU	C	3.98
O3	276-LEU	CB	3.95
O2	276-LEU	CD1	4.03
I1	276-LEU	CD1	4.10
C7	276-LEU	CD2	3.84
C9	276-LEU	CD2	3.73
CII	276-LEU	CD2	4.06
O2	276-LEU	CD2	4.10
03	276-LEU	CD2	3.91
C13	277-SER	N	4.06
C14	277-SER	N	3.13
O4	277-SER	N	3.28
O3	277-SER	N	3.05
C14	277-SER	CA	3.76
O4	277-SER	CA	3.52
C3	277-SER	OG	3.87
C13	277-SER	OG	4.02
C14	277-SER	OG	4.14
I2	290-GLY	0	3.57
I2	292-LEU	CG	3.94
C4	292-LEU	CG	3.95
C6	292-LEU	CG	3.65
C8	292-LEU	CG	4.02
C2	292-LEU	CD1	4.11
C4	292-LEU	CD1	3.85
C6	292-LEU	CD1	4.02
I2	292-LEU	CD2	3.98
C4	292-LEU	CD2	4.11
C6	292-LEU	CD2	3.44
C8	292-LEU	CD2	3.28
C10	292-LEU	CD2	3.88
01	292-LEU	CD2	3.35
I3	299-ILE	CD1	3.77

Triac	Amino Acid	Amino Acid	
Atom	in full length α	Atom	Distance Å
C8	381-HIS	CD2	3.87
C10	381-HIS	CD2	3.90
O1 .	381-HIS	GO2	3.20
O1	381-HIS	CE1	3.82
C8	381-HIS	NE2	3.57
C10	381-HIS	NE2	3.52
O1	381-HIS	NE2	2.64
Ol	388-MET	CE	4.03
01	401-PHE	CE1	3.86
01	401-PHE	CZ	3.70
C13	460-H ₂ 0	01	4.00

Legend to Table 9. The table lists the interactions with Triac. The column headings are as follows:

^{#1} The atom of Triac that interacts with the amino acid of the receptor. These are also 5 numbered in Figure 32.

^{#2} The amino acid in the full length $rTR\alpha$ that interacts with the ligand.

^{#3} The name of the atom in the amino acid (standard nomenclature) where the interaction occurs.

^{#4} The distance in Å between Triac and the protein atom.

Table 10

IpBR ₂ Atom	Amino Acid	Amino Acid	Distance
-p4	in full length α	Atom	Å
C16	215-PHE	CD1	4.01
C16	215-PHE	CEI	3.78
BR1	218-PHE	0	3.24
BR1	218-PHE	C	3.98
C16	218-PHE	CB	3.81
C18	218-PHE	СВ	3.92
BR1	218-PHE	СВ	4.08
C18	218-PHE	CD2	3.92
C16	219-THR	CG2	3.45
BR1	221-ILE	CG1	3.81
BR1	221-ILE	CD1	4.07
BR1	222-ILE	СВ	3.81
BR1	222-ILE	CGI	3.97
C6	222-ILE	CD1	4.07
C8	222-ILE	CD1	3.64
C10	222-ILE	CD1	3.50
C12	222-ILE	CD1	3.82
01	222-ILE	CD1	4.08
C13	225-ALA	СВ	3.76
04	225-ALA	CB	4.01
04	228-ARG	CZ	3.92
C17	228-ARG	NH2	3.26
03	228-ARG	NH2	3.43
04	228-ARG	NH2	2.79
C10	256-MET	SD	3.65
C12	256-MET	SD	3.71
C10	256-MET	CE	3.90
C12	256-MET	CE	3.75
BR2	256-MET	CE	4.03
C11	259-MET	С	3.98
C11	259-MET	0	3.52
C15	259-MET	0	3.44
N1	259-MET	0	3.76
C11	259-MET	СВ	3.87
NI	262-ARG	С	4.03
C15	262-ARG	СВ	4.03
C17	262-ARG	СВ	3.56
03	262-ARG	CB	3.55
04	262-ARG	СВ	3.91
C17	262-ARG	CD	4.09
04	262-ARG	CD	3.71
NI	263-ALA	N	3.61

IpBR ₂ Atom	Amino Acid	Amino Acid	<u>Distance</u>
• -	in full length α	Atom .	Å
N1	263-ALA	CA	3.59
NI	263-ALA	СВ	3.54
03	266-ARG	NH1	3.93
N1	275-THR	0	3.43
N1	276-LEU	CA	3.46
N1	276-LEU	С	3.83
C5	276-LEU	CD1	4.02
C7	276-LEU	CD2	4.00
C9	276-LEU	CD2	3.81
C11	276-LEU	CD2	3.91
C13	277-SER	N	3.79
C15	277-SER	N	3.63
C17	277-SER	N	3.70
NI	277-SER	N	3.17
03	277-SER	N	3.37
C17	277-SER	CA	3.89
03	277-SER	CA	3.43
C13	277-SER	OG	3.66
02	287-LEU	CD1	4.05
C18	290-GLY	C	4.04
C18	290-GLY	0	3.48
C18	291-GLY	CA	4.02
C4	292-LEU	CG	3.89
C6	292-LEU	CG	4.02
C2	292-LEU	CD1	3.79
C4	292-LEU	CD1	3.96
02	292-LEU	CD1	3.97
C4	292-LEU	CD2	4.07
C6	292-LEU	CD2	3.75
C8	292-LEU	CD2	3.67
C10	292-LEU	CD2	3.92
BR2	299-ILE	CD1	3.68
C8	381-HIS	CD2	3.92
C10	381-HIS	CD2	3.78
01	381-HIS	GD2	3.50
01	381-HIS	CE1	3.62
C8	381-HIS	NE2	3.36
C10	381-HIS	NE2	3.34
01	381-HIS	NE2	2.62
C8	401-PHE	CE1	4.02
01	401-PHE	CE1	3.19
C16	401-PHE	CZ	4.03
01	401-PHE	CZ	3.06
03	502-H ₂ O	01	3.40

IpBR ₂ Atom	Amino Acid	Amino Acid	Distance
	in full length α	Atom	Å
N1	502-H20	01	3.12
04	503-H ₂ O	01	3.20
C17	503-H20	01	3.04
03	503-H ₂ O	01	2.27
C15	504-H20	01	4.01
C17	504-H ₂ O	01	2.99
03	504-H2O	01	3.80
04	504-H ₂ O	01	1.78

Legend to Table 10. The table lists the interactions with IpBr2. The column headings are as follows:

- #1 The atom of IpBr2 that interacts with the amino acid of the receptor. These are also 5 numbered in Figure 32.
 - #2 The amino acid in the full length rTRα that interacts with the ligand.
 - #3 The name of the atom in the amino acid (standard nomenclature) where the interaction occurs.
 - #4 The distance in Å between IpBr2 and the protein atom.

Table 11

T3 Atom	Amino Acid	Amino Acid	Distance
. 15 110	in full length α	Atom	Å
12	215-PHE	CD1	4.08
<u> </u>	218-PHE	0	3.19
	218-PHE	CB	3.99
C4	218-PHE	СВ	4.04
II	218-PHE	С	3.79
I1	218-PHE	СВ	3.99
I1	221-ILE	CG1	4.01
I1	222-ILE	СВ	3.95
II	222-ILE	CG1	3.91
C8	222-ILE	CDI	3.99
C10	222-ILE	CD1	3.57
C12	222-ILE	CD1	3.68
C13	225-ALA	СВ	3.66
<u>C3</u>	225-ALA	СВ	4.04
04	228-ARG	NH1	3.23
04	228-ARG	CZ	3.45
C15	228-ARG	NH2	3.54
03	228-ARG	NH2	3.90
04	228-ARG	NH2	2.86
C10	256-MET	SD	3.73
C12	256-MET	SD	3.90
C10	256-MET	CE	3.97
C12	256-MET	CE	3.92
13	256-MET	CE	3.89
C11	259-MET	C	3.95
C11	259-MET	. 0	3.59
C14	259-MET	0	3.51
N1	259-MET	0	3.88
C1	259-MET	CB	4.06
C11	259-MET	CB	3.77
C13	259-MET	CB	3.96
C15	262-ARG	СВ	3.61
C14	262-ARG	CB	4.02
03	262-ARG	СВ	3.65
04	262-ARG	СВ	3.92
04	262-ARG	CD	3.72
N1	263-ALA	N	3.81
NI	263-ALA	CA	3.81
N1	263-ALA	СВ	3.63
NI	275-THR	0	3.54
N1	276-LEU	CA	3.38
NI	276-LEU	С	3.73
C5	276-LEU	CD1	4.00

T3 Atom	Amino Acid	Amino Acid	Distance
	in full length α	Atom	Å
C7	276-LEU	CD1	4.05
02	276-LEU	CD1	4.03
C7	276-LEU	CD2	3.80
C9	276-LEU	CD2	3.70
CII	276-LEU	CD2	4.01
C14	277-SER	N	3.67
C15	277-SER	N ·	3.62
N1	277-SER	N	3.07
03	277-SER	N	3.24
C15	277-SER	CA	3.77
03	277-SER	CA	3.34
C13	277-SER	OG	3.92
12	290-GLY	0	3.50
C4	292-LEU	CG	3.95
C8	292-LEU	CG	3.83
C2	292-LEU	CD1	4.07
C4	292-LEU	CD1	3.99
C4	292-LEU	CD2	4.09
C6	292-LEU	CD2	3.58
C8	292-LEU	CD2	3.50
C10	292-LEU	CD2	3.96
01	292-LEU	CD2	3.71
13	299-ILE	CD1	3.74
C8	381-HIS	CD2	3.94
C10	381-HIS	CD2	3.97
01	381-HIS	CD2	3.39
01	381-HIS	CD1	3.82
C8	381-HIS	NE2	3.47
C10	381-HIS	NE2	3.55
01	381-HIS	NE2	2.70
01	388-MET	ČE	3.88
01	401-PHE	CEI	3.52
01	401-PHE	CZ	3.32
C14	502-H20	01	4.01
C15	502-H2O	O1	3.61
03	502-H20	01	2.51
C15	503-H2O	O1	3.31
04	503-H ₂ O	01	3.10
N1	502-H ₂ O	01	3.27
03	503-H2O	01	2.81
C15	504-H2O	O1	3.92
04	504-H2O	01	2.73

Legend to Table 11. The table lists the interactions with T3. The column headings are as follows:

#1 The atom of T3 that interacts with the amino acid of the receptor. These are also numbered in Figure 32.

- #2 The amino acid in the full length $rTR\alpha$ that interacts with the ligand.
- #3 The name of the atom in the amino acid (standard nomenclature) where the 5 interaction occurs.
 - #4 The distance in Å between T3 and the protein atom.

Table 12

Triac	Amino Acid	Amino Acid	
Atom	in full length hTR β	Atom	Distance Å
I2	269-PHE	CD1	3.75
12	269-PHE	CE1	3.88
11	272-PHE	С	4.03
I1	272-PHE	0	3.54
Ĭ1	275-ILE	CG1	3.93
Il	276-ILE	CG1	4.02
C3	279-ALA	CB	3.81
C13	279-ALA	СВ	3.87
C10	310-MET	SD	3.72
C12	310-MET	SD	3.78
C10	310-MET	CE	4.02
C12	310-MET	CE	3.92
<u>I3</u>	310-MET	CE	3.93
C13	313-MET	CA	3.94
C11	313-MET	С	3.72
C1	313-MET	0	3.79
C11	313-MET	0	3.12
C13	313-MET	Ö	3.55
C1	313-MET	СВ	4.00
C11	313-MET	СВ	3.82
C13	313-MET	CB	3.76
C13	313-MET	CG	3.88
O3	316-ARG	СВ	3.99
O4	317-ALA	CA	4.08
04	317-ALA	CA	4.10
C11	317-ALA	СВ	3.70
I3	317-ALA	CB	4.10
O4	317-ALA	СВ	4.06
O4	320-ARG	NH1	3.58
03	320-ARG	NH2	3.55
04	320-ARG	NH2	4.04
04	329-THR	0	3.55
04	330-LEU	CA	3.42
04	330-LEU	C	3.77
C3	330-LEU	СВ	4.06
C5	330-LEU	СВ	4.08
C1	330-LEU	CD2	4.07
C3	330-LEU	CD2	4.00
C5	330-LEU	CD2	3.73
C7	330-LEU	CD2	3.51
C9	330-LEU	CD2	3.54
C11	330-LEU	CD2	3.86

Triac	Amino Acid	Amino Acid	
Atom	in full length hTR β	Atom	Distance Å
C15	331-ASN	N	3.55
O3	331-ASN	N	3.74
O4	331-ASN	N	3.12
03	331-ASN	CA	4.02
I2	344-GLY	0	3.87
<u>C6</u>	346-LEU	CD2	3.87
C8	346-LEU	CD2	3.84
01	346-LEU	CD2	3.91
13	353-ILE	CD1	3.51
C8	435-HIS	CD2	3.93
C10	435-HIS	CD2	3.79
01	435-HIS	CD2	3.33
01	435-HIS	CEI	3.81
C8	435-HIS	NE2	3.42
C10	435-HIS	NE2	3.33
01	435-HIS	NE2	2.67
01	442-MET	SD	3.96
01	442-MET	CE	3.72
I2	442-MET	SD	4.01
O1	455-PHE	CEI	3.92
01	455-PHE	CZ	3.50

Legend to Table 12. The table lists the interactions with Triac. The column headings are as follows:

^{#1} The atom of Triac that interacts with the amino acid of the receptor. These are also 5 numbered in Figure 32.

^{#2} The amino acid in the full length hTRβ that interacts with the ligand.

^{#3} The name of the atom in the amino acid (standard nomenclature) where the interaction occurs.

^{#4} The distance in Å between Triac and the protein atom.

Table 13

GC1	Amino Acid	Amino Acid	_
Atom	in full length TR β	Atom	Distance Å
C16	269-PHE	CE1	3.99
C19	272-PHE	0	3.85
C16	272-PHE	CB	3.98
C16	273-THR	CG2	3.76
C19	275-ILE	CG1	3.98
C19	276-ILE	CA	3.98
C2	276-ILE	CD1	3.88
C8	276-ILE	CD1	3.77
C10	276-ILE	CD1	· 3.58
C12	276-ILE	CD1	3.62
C19	276-ILE	CD1	3.56
Cl	279-ALA	CB	3.68
C3	279-ALA	CB	3.56
O5	279-ALA	CB	3.11
O4	279-ALA	СВ	3.90
O3	282-ARG	CZ	3.53
C17	282-ARG	NHI	3.87
O3	282-ARG	NH1	3.20
O4	282-ARG	NH1	3.85
C17	282-ARG	NH2	3.63
O3	282-ARG	NH2	3.00
C10	310-MET	SD	3.86
C12	310-MET	SD	3.91
C11	313-MET	С	3.85
C11	313-MET	0	3.41
C15	313-MET	0	3.87
C20	313-MET	0	3.99
C11	313-MET	СВ	3.79
C1	313-MET	CG	3.94
C11	313-MET .	CG	3.91
O5	313-MET	CG	3.87
O4	313-MET	CG	3.79
C20	314-SER	CA	4.00
C17	316-ARG	СВ	3.95
C17	316-ARG	CD	3.80
O3	316-ARG	CD	3.83
O4	316-ARG	CD	3.51
C20	317-ALA	СВ	3.93
C7	330-LEU	CD2	3.56
C9	330-LEU	CD2	3.63
C21	330-LEU	CD2	3.90
O5	331-ASN	N	3.62

GC1	Amino Acid	Amino Acid	_
Atom	in full length TR β	Atom	Distance Å
C15	331-ASN	N	3.67
C18	344-GLY	0	3.60
C18	346-LEU	CG	3.89
C6 .	346-LEU	CD2	3.77
C8	346-LEU	CD2	3.80
C10	435-HIS	CD2	3.89
01	435-HIS	CD2	3.64
01	435-HIS	CEI	3.79
C8	435-HIS	NE2	3.44
C10	435-HIS	NE2	3.33
Ol	435-HIS	NE2	2.77
O1	455-PHE	CE1	3.40
01	455-PHE	CZ	3.22

Legend to Table 13. The table lists the interactions with GC1. The column headings are as follows:

^{#1} The atom of GC1 that interacts with the amino acid of the receptor. These are also 5 numbered in Figure 32.

^{#2} The amino acid in the full length hTRβ that interacts with the ligand.

^{#3} The name of the atom in the amino acid (standard nomenclature) where the interaction occurs.

^{#4} The distance in Å between GC1 and the protein atom.

Table 14
Coordination Structure of TR-α and Dimit

	Coo	rdina	ation S	tructu	re of 1	K-α	and Din				
Coordina-	R ₁	R ₂	R ₃	R ₅	R ₆	R'2	R'3	R'₄	R's	R'6	X
ion			1								
Structure											
	-CH2-CH(NH2)(CO2)H	-H	-CH ₃	-CH ₃	-H	-H	-CH(CH ₃) ₂	-OH	-H	-H	0
AA			1				215				
SS			1				H3				
AA			218				218				
SS	-		H3				H3				
AA							219				
SS							H3				_
AA			221								
SS			H3								
AA			T				222	222	222	222	
SS							Н3	H3	H3	H3	
AA	225										
SS	H3										
AA	228										
SS	H3			Ī							
AA									256	256	
SS									H5-H6	H5-H6	
AA	259				259	ĺ		Ĭ	<u> </u>		
SS	H5-H6				H5-H6]				
AA	262		Ţ								
SS	H5-H6										
AA	263								<u> </u>		
SS	H5-H6							<u> </u>			
AA	266		T		T			<u> </u>			
SS	loop			Ţ				1			
AA	275					l		1			
SS	S3										
AA	276 .		276	276	276				<u> </u>	<u></u>	
SS	S3		S3	S3	S3			L	1		
AĀ	277									<u> </u>	<u> </u>
SS	loop			Ţ			<u> </u>			<u> </u>	
AA							290-291	<u> </u>			L
SS				I			loop			ļ	
AA						292	292	292		ļ	292
SS						loop	loop	loop	loop		loop
AA				299				ļ			<u> </u>
SS				H8				ــــــــــــــــــــــــــــــــــــــ	4	ļ	1
AA							<u> </u>	381		 	
SS						1		HII	HII		1
AA						1	388	1		<u> </u>	<u> </u>
SS							HII			ļ	
AA							401	401		_	1
SS							H12	H12	2	 	
AA	HOH502/HOH503 /HOH504										
SS		1				T					

AA = Amino Acid

SS = Secondary Structure

Coordination	R ₁	R ₂	R ₃	R ₅	R ₆	R'2	R'3	R'₄	R'5	R' ₆	Х
Structure	<u> </u>			<u> </u>							0
	-CH₂-COOH	-H	-I	-1	-H	-H	-I	-OH	-H	-H	0
AA			218			ļ <u> </u>	<u> </u>		ļ		<u> </u>
SS	-		H3			L					<u> </u>
AA			221							ļ	
SS			H3	1		<u> </u>				-	
AA							222	222	222	222	
SS							H3	H3	H3	H3	ļ
AA	225								ļ		
SS	H3			_l			<u> </u>			1	
AA				256		<u> </u>			256	256	ļ
SS				H5-H6		<u> </u>			H5-H6	H5-H6	<u> </u>
AA	259				259	<u> </u>			<u> </u>		<u> </u>
SS	Н5-Н6		J		H5-H6				<u> </u>		<u> </u>
AA	262										ļ
SS	H5-H6			Ī							<u> </u>
AA	263						ļ		<u> </u>	ļ	<u> </u>
SS	H5-H6									<u> </u>	<u> </u>
AA	266										<u>.</u>
SS	loop				l		<u> </u>	<u> </u>			<u> </u>
AA	275				<u> </u>		<u> </u>				<u> </u>
SS	S3	Ī				1				<u> </u>	
AA	276		276	276	276						ļ
SS	S3		S3	S3	S3		<u> </u>		<u> </u>		
AA	277										
SS	loop									<u> </u>	
AA					Ī		290	L		<u> </u>	<u> </u>
SS							loop				<u> </u>
AA						292	292	292	292		292
SS		1				loop	loop	loop	loop		loop
AA				299							<u> </u>
SS				H8							
AA								381	381		
SS					1			HII	H11		
AA		1			,			388			<u></u>
SS								H11			
AA		1					401	401			
SS		1					H12	H12			

5 AA = Amino Acid SS = Secondary Structure

							and IpB		D'	ים י	Х
Coordina-	Ri	R ₂	R ₃	R ₅	R ₆	R'2	R'3	R' ₄	R's	R'6	^
tion											
Structure						 -	-CH(CH ₃) ₂	OU	-H	-H	0
	-CH ₂ -CH(NH ₂)(CO ₂)H	-H	-Br	-Br	-H	-H		-OH	-H	-H	
AA							215			ļ	
SS							H3				
AA			218				218				
SS			Н3				H3			ļ	
AA							219				
SS							Н3				
AA			221								
SS			Н3								<u> </u>
AA							222	222	222	222	<u> </u>
SS							H3	H3	Н3	H3	
AA	225										
SS	H3										
AA	228									L	l
SS	Н3										
AA					256	<u> </u>			256	256	
SS					H5-H6				H5-H6	H5-H6	
AA	259				259	İ					
SS	H5-H6				H5-H6	L	<u></u>	L			
AA	262	[<u> </u>				
SS	H5-H6					<u> </u>		<u> </u>			
AA	263							<u> </u>			
SS	H5-H6						ļ <u>.</u>	<u> </u>			
AA	266										<u> </u>
SS	loop							1			
AA	275										
SS	S3									<u> </u>	<u> </u>
AA	276		276	276	276						
SS	S3		S3	S3	S3				İ	<u></u>	
AA	277										
SS					ľ						<u> </u>
AA							290-291	<u> </u>	<u> </u>	<u> </u>	
SS							loop	<u> </u>		<u> </u>	
AA						292	292	292	292		292
SS.						loop	loop	loop	loop	<u> </u>	loop
AA				299							<u> </u>
SS				H8						l	
AA		T						381	381		
SS		T						HII	HII		
AA			1				401	401			
SS							H12	H12			
AA	HOH502/HOH503/ HOH504										
SS				1	1		1			1	1

AA = Amino Acid

SS = Secondary Structure

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Coordination	R _i	R ₂	R ₃	R ₅	R ₆	R'2	R'3	R'₄	R'5	R'6	X
Structure	-CH ₂ -CH(NH ₂)(CO ₂)H	-H	-l	I	-H	-H	-I	-ОН	-H	-H	0
	-Cnj-Cn(ivii)(CO)(i	-17	-1	-1	-n	-11	215	-0.1			
AA							H3				-,
SS			218			218	-115				
AA			H3			H3					
SS	-		221			пэ					
AA			H3								
SS		ļ	н3				222	222	222	222	
AA		_	.				H3	H3	H3	H3	
SS		L	ļ				нэ	כח	כח	כח	
AA	225	<u> </u>									
SS	H3			ļ						· · · · · · · · · · · · · · · · · · ·	
AA	228		ļ	ļ	ļ						
SS	H3	ļ	1						256	256	
AA					256				256	256	
SS					H5-H6				H5-H6	H5-H6	
AA	259		<u> </u>		259		<u> </u>				
SS	Н5-Н6	L			H5-H6			<u> </u>			
AA	262	<u> </u>									<u> </u>
SS	H5-H6	<u> </u>	<u> </u>								
AA	263	Ī		<u> </u>				<u> </u>	ļ		
SS	Н5-Н6		<u> </u>					ļ		ļ	
AA	275		1	<u> </u>	<u> </u>			<u> </u>		<u> </u>	
SS	S3			<u> </u>	1			ļ			ļ
AA	276		276	276	276		<u> </u>	ļ			
SS	S3	Ţ	S3	S3	S3		<u> </u>	<u> </u>		<u> </u>	
AA	277						<u> </u>	<u></u>	<u> </u>		<u> </u>
SS						<u> </u>	<u> </u>	L	<u> </u>	<u> </u>	
AA		1					290				
SS		T					loop	<u> </u>		<u> </u>	
AA						292	292	292	292		292
SS			1	}	T	loop	loop	loop	loop		loop
AA		T		299					1		
SS		T"		H8							
AA		T						381	381		
SS		1	\top			<u> </u>		HII	H11		
AA			1		Ţ	·		388			
SS				7		1		Hll			<u> </u>
AA		\top		1	1	T	401	401			
SS				1	1	T	H12	H12			
AA	HOH502/H0H503/ HOH504										
SS			d C								

AA = Amino Acid SS = Secondary Structure

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Table 18 Coordination Structure of TR- β and Triac

Coordination	RI	R2	R3	R5	R6	R2'	R3	R4	R5	R6	X
Structure	1										
	-CH ₂ CO ₂ H	Н	I	I	Н	Н	1	OH	Н	Н	0
AA							269				
SS							Н3				
AA			272								
SS	1		Н3								
AA			275								
SS			H3								
AA			276								
SS			H3								
AA	279	279									
SS	H3	H3									
AA	1			310					310	310	
SS	1			H5-H6		1			H5-H6	H5-H6	
AA	313	1			313						
SS	H5-H6				H5-H6						
AA	316										
SS	H5-H6			İ							
AA	317	ĺ			317		317				,
SS	H5-H6				H5-H6		H5-H6				
AA	320	 									
SS	H5-H6	<u> </u>	ļ								
AA	329						<u> </u>				
SS	S3		<u> </u>								
AA	330	330	330	330	330						
SS	S3	S3	S3	S3	S3						
AA	331	1									
SS	loop										
AA	- -		1				344				П
SS	<u> </u>	1		-	1	1	loop				
AA		1	1				346	346			
SS				1	1	\vdash	loop	loop			1
AA	1	†	1	353		—					
SS	 	†	1	H8			1		T		\Box
AA	-		 				 	435	435		
SS	<u> </u>	1	1	1				HII	HII		T
AA	 	1	\top	1		1	442	442			T
SS		1 -	1	T	1	1	H11	HII			T
AA		- 	_	1	 	╁┈╌	 	455			T
SS			+	 	1	1		H12			T

AA = Amino Acid SS = Secondary Structure

Table 19
Coordination Structure of TR-β and GC1

							B and GC				
Coordina-	Rı	R ₂	R ₃	R ₅	R ₆	R2	R3	R4	R5	R6	X
tion							,	- 1			
Structure											
	-O-CH ₂ CO ₂ H	Н	CH ₃	CH ₃	Н	Н	CH(CH ₃)	OH	Н	Н	CH ₂
AA							269				
SS							H3				
AA			272								
SS			H3								
AA			273				273				
SS			H3				H3				
AA			275								
SS			H3				<u></u>				
AA			276			L		276	276	276	
SS			H3				<u> </u>	H3	Н3	H3	<u> </u>
AA	279	279	Ī				L				
SS	H3	H3									
AA	282	[
AA SS	H3										<u></u>
AA				310					310	310	<u>.</u>
SS				H5-H6					H5- H6	Н5-Н6	
AA	313	<u> </u>	1		313						
SS	H5-H6		1		H5-H6						
AA		 	1				314				
SS		<u> </u>	1		<u> </u>		H5-H6				
AA	316		1		<u> </u>						
SS	H5-H6	1	1								
AA							317				
SS	 	1	1				H5-H6				
AA	320		†								
SS	H5-H6	 	†			1					
AA	329		1		-						
SS	S3	1	1	<u> </u>							
AA	330	 	1	330							
SS	S3	†	+	S3	†			T			
AA	331	1	†		1						
SS	loop	1	1 -	T		 	1	1			
AA	 		1	†		1	344	1			
SS		†	+			1	loop	1	T		
AA	-	1	1	T	1	1	346	346			
SS		+	+	 	+	\top	loop	loop	1	1	T
AA	1	 	_	353	1	\top	 	T	1		
SS	-	1-	+	H8	+	1-				T	1
AA		+	+	1	+		-	435	435	1	\top
	 	+	 	1	+	+-		HII	HII	1	1
	 	+	+	1	 	+-	1	455		1	
SS			+	+	+	+		H12			

AA = Amino Acid

SS = Secondary Structure

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APPENDIX 3

TR_DMT.PDB

REMARK TR_dmt full length numbering

REMARK

5 REMARK Rfactor 0.205 Rfree 0.227

REMARK Resolution 15. 2.2 all reflections

REMARK

REMARK Three cacodylate-modified cysteines (CYA)

REMARK Cya334, Cya380, Cya392

10 REMARK cacodylate modeled as single arsenic atom

REMARK

REMARK side chain of certain residues modeled as ALA due to poor density;

REMARK however, residue name reflects true residue for clarity

REMARK

15 REMARK clone obtained from Murray et. al.

REMARK deposited sequence confirmed,

REMARK differing from that reported by Thompson et. al.

REMARK in the following codons:

REMARK 281 Thr - Ala

20 REMARK 285 Lys - Glu

REMARK identical to that reported by Mitsuhashi et. al.

REMARK gb:RNTRAVI X07409

JRNL

45

AUTH

M.B. MURRAY, N.D.ZILZ,

N.L.MCCREARY, M.J.MACDONALD

25 JRNL AUTH 2 H.C.TOWLE

JRNL TITL ISOLATION AND CHARACTERIZATION OF RAT CDNA CLONES FOR TWO

JRNL TITL 2 DISTINCT THYROID HORMONE RECPTORS

JRNL REF JBC

V. 263 25 1988

JRNL AUTH C.C.THOMPSON, C.WEINBERGER, R.LEBO, R.M.EVANS JRNL TITL IDENTIFICATION OF A NOVEL THYROID HORMONE RECEPTOR EXPRESSED

JRNL TITL 2 IN THE MAMMALIAN CENTRAL NERVOUS SYSTEM

JRNL REF SCIENCE

V. 237 1987

35 JRNL AUTH T.MITSUHASHI,G.TENNYSON,V.NIKODEM

BNI TITI NUCLEOTIDE SEQUENCE OF NOVEL CDNAS

JRNL TITL NUCLEOTIDE SEQUENCE OF NOVEL CDNAS GENERATED BY ALTERNATIVE

JRNL TITL 2 SPLICING OF A RAT THYROID HORMONE RECEPTOR GENE TRANSCRIPT

40 JRNL REF NUC. ACIDS. RES. V. 16 12 1988

ATOM 1 N ARG 157 68.504 8.445 5.651 1.00 68.93

ATOM 2 CA ARG 157 67.886 9.543 6.398 1.00 56.98

ATOM 3 CB ARG 157 68.769 10.789 6.324 1.00 59.25

ATOM 4 CG ARG 157 70.147 10.632 6.932 1.00 58.90

ATOM 5 CD ARG 157 70.068 10.422 8.425 1.00 59.37 ATOM 6 NE ARG 157 71.392 10.446 9.036 1.00 63.94

ATOM 7 CZ ARG 157 71.613 10.329 10.341 1.00 64.39

ATOM 8 NH1 ARG 157 70.596 10.182 11.179 1.00 62.14

PCT/US98/25296

```
72.855 10.365 10.808 1.00 65.56
             9 NH2 ARG 157
    ATOM
                              66.500 9.881 5.854 1.00 48.97
            10 C ARG 157
    ATOM
                              66.351 10.203 4.674 1.00 48.61
            11 O ARG 157
    ATOM
                              65.469 9.818 6.712 1.00 41.90
            12 N PRO 158
    ATOM
                               65.550 9.366 8.112 1.00 41.06
            13 CD PRO 158
5
    ATOM
                               64.083 10.114 6.333 1.00 39.34
            14 CA PRO 158
    ATOM
                               63.286 9.704 7.576 1.00 37.89
            15 CB PRO 158
    ATOM
                               64.260 9.883 8.693 1.00 42.40
             16 CG PRO 158
    ATOM
                              63.814 11.573 5.930 1.00 37.10
            17 C PRO 158
    ATOM
                              64.189 12.517 6.636 1.00 33.31
             18 O PRO 158
10
    ATOM
                              63.171 11.733 4.778 1.00 30.56
            19 N GLU 159
    ATOM
                               62.821 13.038 4.231 1.00 24.26
    ATOM
             20 CA GLU 159
                               62.553 12.904 2.727 1.00 19.19
            21 CB GLU 159
    ATOM
                               63.788 12.677 1.874 1.00 20.60
            22 CG GLU 159
    ATOM
                               64.407 13.971 1.390 1.00 26.54
15
    ATOM
            23 CD GLU 159
    ATOM
            24 OE1 GLU 159
                               63.649 14.929 1.115 1.00 30.85
                               65.649 14.027 1.268 1.00 28.35
            25 OE2 GLU 159
    ATOM
                              61.549 13.520 4.909 1.00 23.26
             26 C GLU 159
    ATOM
                              60.906 12.765 5.643 1.00 26.86
            27 O GLU 159
     ATOM
                              61.200 14.806 4.729 1.00 22.72
    ATOM
             28 N PRO 160
20
                               61.981 15.916 4.153 1.00 17.87
             29 CD PRO 160
    ATOM
                               59.969 15.292 5.359 1.00 19.90
             30 CA PRO 160
     ATOM
                               60.004 16.799 5.070 1.00 14.42
             31 CB PRO 160
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                               61.465 17.109 4.919 1.00 12.87
     ATOM
             32 CG PRO 160
                              58.747 14.623 4.701 1.00 23.68
             33 C PRO 160
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                              58.730 14.383 3.491 1.00 24.72
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                               55.691 13.031 6.125 1.00 21.50
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                                55.163 14.062 6.972 1.00 20.33
             38 OG1 THR 161
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             39 CG2 THR 161
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                              55.744 14.765 4.298 1.00 22.86
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                              56.040 15.949 4.481 1.00 27.68
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             41 O THR 161
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                               54.280 13.050 3.113 1.00 16.55
             43 CD PRO 162
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     ATOM
                               53.924 15.435 2.830 1.00 21.97
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             44 CA PRO 162
                               52.780 14.633 2.210 1.00 18.17
             45 CB PRO 162
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                               53.422 13.316 1.905 1.00 18.01
             46 CG PRO 162
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                              53,399 16,467 3,826 1,00 22,56
             47 C PRO 162
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                              53.461 17.675 3.567 1.00 21.73
             48 O PRO 162
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                               52.912 15.976 4.967 1.00 25.28
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                               52.357 16.816 6.030 1.00 26.64
             50 CA GLU 163
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                               51.743 15.962 7.144 1.00 30.22
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             51 CB GLU 163
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             52 CG GLU 163
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             53 CD GLU 163
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                                50.016 13.660 4.929 1.00 52.48
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             54 OE1 GLU 163
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             55 OE2 GLU 163
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             62 CD GLU 164
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             64 OE2 GLU 164
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             66 O GLU 164
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             68 CA TRP 165
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             70 CG TRP 165
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             73 CE3 TRP 165
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             74 CD1 TRP 165
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             75 NE1 TRP 165
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             77 CZ3 TRP 165
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             78 CH2 TRP 165
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             80 O TRP 165
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                               53.369 21.796 4.621 1.00 25.77
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             86 OD2 ASP 166
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                               54.439 22.640 8.187 1.00 28.28
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             91 CB LEU 167
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             93 CD1 LEU 167
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             94 CD2 LEU 167
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                               55.636 23.532 7.902 1.00 22.19
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             95 C LEU 167
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             98 CA ILE 168
                               57.846 23.632 6.833 1.00 18.03
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             99 CB ILE 168
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            100 CG2 ILE 168
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            101 CG1 ILE 168
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            102 CD1 ILE 168
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                              57.579 24.897 6.022 1.00 22.54
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            103 C ILE 168
            104 O ILE 168
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                               56.682 24.800 5.045 1.00 25.70
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                               56.337 25.934 4.190 1.00 21.28
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                               55.411 25.493 3.057 1.00 22.29
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            107 CB HIS 169
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     ATOM 108 CG HIS 169
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            112 NE2 HIS 169
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            114 O HIS 169
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            115 N VAL 170
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                               53.957 27.661 6.607 1.00 21.29
            116 CA VAL 170
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                               52.808 26.991 7.399 1.00 24.33
            117 CB VAL 170
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                                52.164 27.985 8.354 1.00 23.78
            118 CG1 VAL 170
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                                51.760 26.439 6.435 1.00 18.87
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            120 C VAL 170
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            123 CA ALA 171
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            124 CB ALA 171
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            125 C ALA 171
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            130 OG1 THR 172
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            132 C THR 172
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            137 CG GLU 173
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            138 CD GLU 173
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            139 OE1 GLU 173
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            146 C ALA 174
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            147 O ALA 174
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            151 CG HIS 175
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            152 CD2 HIS 175
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            153 ND1 HIS 175
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            154 CE1 HIS 175
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     ATOM 155 NE2 HIS 175
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     ATOM 156 C HIS 175
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            161 CG ARG 176
    ATOM
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            162 CD ARG 176
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                               62.316 32.477 2.813 1.00 58.20
           163 NE ARG 176
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                               62.266 31.548 1.867 1.00 67.22
           164 CZ ARG 176
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           165 NH1 ARG 176
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           167 C ARG 176
                              60.073 37.760 6.209 1.00 24.52
           168 O ARG 176
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10
                              58.177 36.598 6.515 1.00 23.60
           169 N SER 177
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                               57.341 37.789 6.565 1.00 26.36
    ATOM
           170 CA SER 177
           171 CB SER 177
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                               55.495 36.459 7.423 1.00 25.97
           172 OG SER 177
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           173 C SER 177
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           174 O SER 177
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           178 OG1 THR 178
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           179 CG2 THR 178
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           180 C THR 178
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           181 O THR 178
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           183 CA ASN 179
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           187 ND2 ASN 179
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           192 CB ALA 180
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    ATOM
           198 CG GLN 181
            199 CD GLN 181
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    ATOM 200 OE1 GLN 181
    ATOM 201 NE2 GLN 181
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    ATOM 202 C GLN 181
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                               66.181 42.291 4.251 1.00 46.47
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            203 O GLN 181
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            204 N GLY 182
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                               65.054 39.815 4.742 1.00 42.63
            205 CA GLY 182
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            206 C GLY 182
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     ATOM
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     ATOM 208 N SER 183
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68.189 39.061 2.733 1.00 54.13 ATOM 209 CA SER 183 68.208 38.225 1.449 1.00 55.08 ATOM 210 CB SER 183 67.197 38.647 0.546 1.00 63.54 211 OG SER 183 ATOM 68.949 40.369 2.532 1.00 54.84 212 C SER 183 ATOM 70.175 40.373 2.407 1.00 56.90 213 O SER 183 5 ATOM 68,223 41.482 2.535 1.00 55.77 ATOM 214 N HIS 184 68.854 42.775 2.342 1.00 57.78 215 CA HIS 184 ATOM 69.605 43.296 3.556 1.00 59.09 216 C HIS 184 ATOM 70.312 44.301 3.454 1.00 60.34 217 O HIS 184 ATOM 69.502 42.597 4.686 1.00 55.60 218 N TRP 185 10 ATOM 70.159 43.020 5.923 1.00 53.73 219 CA TRP 185 ATOM 69.973 41.973 7.030 1.00 50.40 ATOM 220 CB TRP 185 70.746 40.694 6.837 1.00 48.09 221 CG TRP 185 ATOM 72.091 40.419 7.269 1.00 47.38 222 CD2 TRP 185 ATOM 72.390 39.094 6.888 1.00 40.29 15 ATOM 223 CE2 TRP 185 73.071 41.169 7.937 1.00 45.43 224 CE3 TRP 185 ATOM 70.301 39.554 6.234 1.00 49.87 225 CD1 TRP 185 ATOM ATOM 226 NE1 TRP 185 71.280 38.589 6.262 1.00 48.02 73.628 38.496 7.154 1.00 38.65 ATOM 227 CZ2 TRP 185 74.304 40.573 8.201 1.00 43.26 ATOM 228 CZ3 TRP 185 20 ATOM 229 CH2 TRP 185 74.570 39.250 7.807 1.00 40.00 71.638 43.386 5.800 1.00 55.99 ATOM 230 C TRP 185 72.089 44.359 6.401 1.00 52.84 ATOM 231 O TRP 185 72.389 42.614 5.021 1.00 59.15 ATOM 232 N LYS 186 73.818 42.863 4.843 1.00 64.01 233 CA LYS 186 25 ATOM 74.466 41.688 4.091 1.00 64.67 ATOM 234 CB LYS 186 75.943 41.868 3.729 1.00 65.58 ATOM 235 CG LYS 186 76.817 42.181 4.946 1.00 62.03 ATOM 236 CD LYS 186 78.238 42.512 4.515 1.00 61.52 237 CE LYS 186 ATOM 78.988 43.243 5.579 1.00 61.67 ATOM 238 NZ LYS 186 30 74.131 44.203 4.160 1.00 67.49 ATOM 239 C LYS 186 75.164 44.816 4.432 1.00 68.66 ATOM 240 O LYS 186 73.221 44.678 3.316 1.00 68.99 ATOM 241 N GLN 187 73.431 45.939 2.612 1.00 69.65 ATOM 242 CA GLN 187 72.880 45.867 1.180 1.00 73.76 243 CB GLN 187 35 ATOM 73.632 44.935 0.237 1.00 78.61 ATOM 244 CG GLN 187 73,368 43,471 0.525 1.00 84.96 ATOM 245 CD GLN 187 ATOM 246 OE1 GLN 187 74.203 42.782 1.109 1.00 87.73 72.197 42.989 0.122 1.00 84.98 ATOM 247 NE2 GLN 187 72.817 47.141 3.323 1.00 69.16 248 C GLN 187 40 ATOM 73.379 48.235 3.299 1.00 71.39 **ATOM** 249 O GLN 187 71.666 46.936 3.953 1.00 65.82 ATOM 250 N ARG 188 70.961 48.014 4.639 1.00 65.00 251 CA ARG 188 ATOM 69.458 47.739 4.591 1.00 66.20 252 CB ARG 188 ATOM 68.957 47.483 3.181 1.00 70.30 ATOM 253 CG ARG 188 45 67.463 47.212 3.132 1.00 78.59 ATOM 254 CD ARG 188 67.003 47.008 1.760 1.00 87.71 ATOM 255 NE ARG 188 67.011 47.946 0.814 1.00 94.10 ATOM 256 CZ ARG 188 67.453 49.171 1.081 1.00 97.26 ATOM 257 NH1 ARG 188 66.589 47.657 -0.409 1.00 94.07 ATOM 258 NH2 ARG 188 50

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71.409 48.286 6.077 1.00 65.39
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            260 O ARG 188
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           263 CB ARG 189
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            266 NE ARG 189
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            267 CZ ARG 189
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            268 NH1 ARG 189
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           270 C ARG 189
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    ATOM
            273 CA LYS 190
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            274 CB LYS 190
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           275 C LYS 190
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    ATOM 276 O LYS 190
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           278 CA PHE 191
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           282 CD2 PHE 191
           283 CE1 PHE 191
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           284 CE2 PHE 191
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                               80.158 47.311 9.646 1.00 48.48
           285 CZ PHE 191
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                              76.663 51.534 13.248 1.00 48.61
           286 C PHE 191
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     ATOM 287 O PHE 191
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     ATOM 289 CA LEU 192
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     ATOM 291 CG LEU 192
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     ATOM 292 CD1 LEU 192
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           293 CD2 LEU 192
     ATOM
35
                              77.447 52.760 15.800 1.00 42.28
     ATOM 294 C LEU 192
     ATOM 295 O LEU 192
                               78.528 52.179 15.932 1.00 39.71
                               77.350 54.104 15.781 1.00 45.15
     ATOM 296 N PRO 193
                               76.095 54.865 15.617 1.00 43.82
     ATOM 297 CD PRO 193
                               78.493 55.006 15.973 1.00 43.14
     ATOM 298 CA PRO 193
40.
                               77.820 56.306 16.400 1.00 44.37
            299 CB PRO 193
     ATOM
                               76.571 56.308 15.565 1.00 41.66
     ATOM 300 CG PRO 193
                               79.476 54.498 17.028 1.00 43.34
     ATOM
            301 C PRO 193
                               79.103 54.296 18.182 1.00 45.18
            302 O PRO 193
     ATOM
            303 N ASP 194
                              80.732 54.317 16.628 1.00 44.22
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     ATOM
                               81.781 53.804 17.512 1.00 47.20
     ATOM
            304 CA ASP 194
                               83.108 53.732 16.761 1.00 41.89
            305 CB ASP 194
     ATOM
                              81.962 54.511 18.866 1.00 51.99
            306 C ASP 194
     ATOM
                              82.636 53.986 19.752 1.00 54.04
            307 O ASP 194
     ATOM
                              81.381 55.698 19.025 1.00 55.21
     ATOM 308 N ASP 195
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81.489 56.428 20.288 1.00 57.50
            309 CA ASP 195
    ATOM
                               81.423 57.948 20.061 1.00 60.04
            310 CB ASP 195
    ATOM
                               80.123 58.398 19.406 1.00 68.39
           311 CG ASP 195
    ATOM
                               79.211 58.847 20.136 1.00 69.46
            312 OD1 ASP 195
    ATOM
            313 OD2 ASP 195
                                80.020 58.322 18.162 1.00 72.91
    ATOM
                              80.410 55.976 21.280 1.00 58.05
           314 C ASP 195
    ATOM
                              80.540 56.180 22.491 1.00 58.97
           315 O ASP 195
    ATOM
                              79.349 55.363 20.759 1.00 56.06
           316 N ILE 196
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                              78.247 54.863 21.580 1.00 50.48
           317 CA ILE 196
    ATOM
                              76.930 54.762 20.766 1.00 45.82
           318 CB ILE 196
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    ATOM
                               75.818 54.166 21.621 1.00 44.04
    ATOM
           319 CG2 ILE 196
    ATOM 320 CG1 ILE 196
                               76.517 56.147 20.261 1.00 44.27
    ATOM 321 CD1 ILE 196
                               75.179 56.171 19.541 1.00 45.25
                             78.603 53.484 22.135 1.00 47.66
    ATOM 322 C ILE 196
                              79.138 52.636 21.419 1.00 43.96
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    ATOM 323 O ILE 196
                               78.309 53.269 23.414 1.00 46.29
    ATOM 324 N GLY 197
           325 CA GLY 197
                               78.608 51.995 24.045 1.00 48.03
    ATOM
                              79.978 51.963 24.692 1.00 50.42
    ATOM 326 C GLY 197
            327 O GLY 197
                               80.463 50.902 25.070 1.00 46.66
    ATOM
                               80.583 53.137 24.854 1.00 56.94
           328 N GLN 198
20
    ATOM
                               81.910 53.259 25.454 1.00 59.51
           329 CA GLN 198
    ATOM
           330 CB GLN 198
                               82.751 54.257 24.649 1.00 62.53
    ATOM
                                83.232 53.718 23.316 1.00 69.39
    ATOM 331 CG GLN 198
                                84.088 52.484 23.483 1.00 76.76
    ATOM 332 CD GLN 198
                                83.745 51.399 22.996 1.00 81.73
     ATOM 333 OE1 GLN 198
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     ATOM 334 NE2 GLN 198
                                85.205 52.632 24.192 1.00 78.09
                               81.915 53.678 26.922 1.00 57.56
    ATOM 335 C GLN 198
                               82.946 53.584 27.588 1.00 57.71
     ATOM 336 O GLN 198
                              80.770 54.128 27.425 1.00 54.11
     ATOM 337 N SER 199
                               80.676 54.600 28.800 1.00 46.28
     ATOM 338 CA SER 199
30
                               80.243 56.067 28.777 1.00 50.28
    ATOM
            339 CB SER 199
                               80.935 56.776 27.757 1.00 50.95
            340 OG SER 199
     ATOM
                              79.776 53.805 29.757 1.00 40.19
            341 C SER 199
     ATOM
                              78.680 54.252 30.102 1.00 39.26
     ATOM 342 O SER 199
                               80.236 52.629 30.214 1.00 35.63
            343 N PRO 200
     ATOM
35
     ATOM 344 CD PRO 200
                               81.530 52.011 29.904 1.00 34.88
                                79.464 51.789 31.139 1.00 37.54
     ATOM 345 CA PRO 200
                               80.223 50.457 31.124 1.00 29.86
            346 CB PRO 200
     ATOM
                                81.207 50.570 29.995 1.00 34.29
     ATOM 347 CG PRO 200
            348 C PRO 200
                               79.521 52.416 32.532 1.00 44.63
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     ATOM
                               80.443 52.137 33.300 1.00 47.80
            349 O PRO 200
     ATOM
                              78.532 53.241 32.867 1.00 49.57
            350 N ILE 201
     ATOM
                               78.525 53.924 34.158 1.00 49.15
     ATOM
            351 CA ILE 201
            352 CB ILE 201
                               78.213 55.426 33.990 1.00 49.19
     ATOM
                               78.429 56.150 35.306 1.00 53.37
            353 CG2 ILE 201
45
     ATOM
                               79.137 56.037 32.934 1.00 52.55
     ATOM 354 CG1 ILE 201
                               78.811 57.471 32.586 1.00 55.26
     ATOM
            355 CD1 ILE 201
            356 C ILE 201
                              77.625 53.352 35.254 1.00 49.88
     ATOM
                              78.044 53.250 36.408 1.00 50.20
            357 O ILE 201
     ATOM
                              76.384 53.014 34.920 1.00 47.85
            358 N VAL 202
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     ATOM
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ATOM 359 CA VAL 202
                               75.468 52.474 35.927 1.00 45.76
                               74.015 52.415 35.400 1.00 39.98
            360 CB VAL 202
    ATOM
            361 CG1 VAL 202
                               73.072 51.896 36.482 1.00 35.94
    ATOM
                               73.574 53.799 34.944 1.00 29.43
    ATOM 362 CG2 VAL 202
                              75.954 51.093 36.373 1.00 50.57
    ATOM 363 C VAL 202
5
            364 O VAL 202
                              76.296 50.249 35.545 1.00 49.50
    ATOM
                              76.009 50.876 37.683 1.00 54.82
            365 N SER 203
    ATOM
                              76.490 49.609 38.223 1.00 59.26
           366 CA SER 203
    ATOM
                              77.067 49.809 39.628 1.00 64.88
    ATOM 367 CB SER 203
                               76.127 50.428 40.492 1.00 75.47
    ATOM 368 OG SER 203
10
                              75.457 48.491 38.244 1.00 55.78
    ATOM 369 C SER 203
                              74.285 48.712 38.544 1.00 57.50
    ATOM
            370 O SER 203
                              75.923 47.283 37.958 1.00 52.29
            371 N MET 204
    ATOM
                               75.076 46.103 37.948 1.00 50.42
            372 CA MET 204
    ATOM
                               75.032 45.487 36.548 1.00 47.74
           373 CB MET 204
    ATOM
15
                               74.243 46.297 35.541 1.00 43.40
           374 CG MET 204
    ATOM
           375 SD MET 204
                               72.491 46.348 35.953 1.00 40.93
    ATOM
           376 CE MET 204
                               71.947 44.785 35.241 1.00 39.19
    ATOM
           377 C MET 204
                              75.670 45.107 38.925 1.00 49.42
    ATOM
                              76.892 45.020 39.062 1.00 52.25
    ATOM 378 O MET 204
20
                              74.816 44.329 39.605 1.00 47.73
    ATOM 379 N PRO 205
    ATOM 380 CD PRO 205
                               73.344 44.414 39.549 1.00 48.94
    ATOM 381 CA PRO 205
                              75.250 43.326 40.580 1.00 47.34
                               73.982 42.513 40.810 1.00 49.44
     ATOM 382 CB PRO 205
                               72.907 43.562 40.725 1.00 50.62
     ATOM 383 CG PRO 205
25
    ATOM 384 C PRO 205
                              76.431 42.442 40.168 1.00 47.12
                              77.299 42.160 40.990 1.00 51.21
     ATOM 385 O PRO 205
                              76.487 42.023 38.909 1.00 48.81
           386 N ASP 206
     ATOM
                               77.583 41.160 38.465 1.00 49.88
           387 CA ASP 206
     ATOM
                               77.128 40.223 37.330 1.00 54.06
     ATOM 388 CB ASP 206
30
                               76.598 40.967 36.107 1.00 57.34
           389 CG ASP 206
     ATOM
                               77.056 42.095 35.811 1.00 52.21
     ATOM 390 OD1 ASP 206
                                75.719 40.397 35.423 1.00 59.16
     ATOM 391 OD2 ASP 206
                              78.902 41.843 38.093 1.00 48.70
     ATOM 392 C ASP 206
                              79.862 41.171 37.715 1.00 49.75
     ATOM 393 O ASP 206
35
                               78.946 43.168 38.161 1.00 47.54
           394 N GLY 207
     ATOM
           395 CA GLY 207
                               80.174 43.869 37.820 1.00 49.23
     ATOM
                              80.169 44.585 36.482 1.00 51.96
           396 C GLY 207
     ATOM
           397 O GLY 207
                               80.783 45.645 36.348 1.00 56.32
     ATOM
                              79.510 44.005 35.481 1.00 52.50
40
     ATOM 398 N ASP 208
     ATOM 399 CA ASP 208
                               79.435 44.624 34.157 1.00 48.00
                               78.968 43.609 33.115 1.00 53.23
            400 CB ASP 208
     ATOM
     ATOM 401 CG ASP 208
                               80.038 42.592 32.774 1.00 53.17
                                81.130 43.006 32.335 1.00 57.42
     ATOM 402 OD1 ASP 208
            403 OD2 ASP 208
                                79.787 41.380 32.942 1.00 55.64
     ATOM
45
                              78.497 45.823 34.187 1.00 46.68
     ATOM 404 C ASP 208
                              77.283 45.671 34.332 1.00 45.81
     ATOM 405 O ASP 208
                              79.075 47.014 34.077 1.00 45.95
     ATOM 406 N LYS 209
                               78.313 48.257 34.115 1.00 45.87
     ATOM 407 CA LYS 209
                               79.235 49.418 34.478 1.00 46.90
     ATOM 408 CB LYS 209
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	ATOM	409 C LYS 209	77.561 48.546 32.812 1.00 41.17
	ATOM	410 O LYS 209	77.951 48.074 31.745 1.00 39.51
	ATOM	411 N VAL 210	76.500 49.344 32.916 1.00 39.35
	ATOM	412 CA VAL 210	75.652 49.713 31.782 1.00 38.03
5	ATOM	413 CB VAL 210	74.136 49.584 32.140 1.00 32.13
	ATOM	414 CG1 VAL 210	73.269 49.926 30.937 1.00 27.92
	ATOM	415 CG2 VAL 210	73.818 48.183 32.627 1.00 29.43
	ATOM	416 C VAL 210	75.895 51.134 31.263 1.00 38.68
	ATOM	417 O VAL 210	76.090 52.079 32.038 1.00 39.57
10	ATOM	418 N ASP 211	75.848 51.272 29.942 1.00 39.19
	ATOM	419 CA ASP 211	76.019 52.544 29.254 1.00 38.39
	ATOM	420 CB ASP 211	76.794 52.327 27.946 1.00 40.36
	ATOM	421 CG ASP 211	77.051 53.620 27.177 1.00 36.85
	ATOM	422 OD1 ASP 211	76.193 54.528 27.167 1.00 37.95
15	ATOM	423 OD2 ASP 211	78.121 53.716 26.553 1.00 33.87
	ATOM	424 C ASP 211	74.601 53.040 28.958 1.00 40.60
	ATOM ·	425 O ASP 211	73.919 52.517 28.073 1.00 40.36
	ATOM	426 N LEU 212	74.185 54.074 29.680 1.00 41.55
	ATOM	427 CA LEU 212	72.854 54.664 29.552 1.00 38.39
20	ATOM	428 CB LEU 212	72.759 55.883 30.467 1.00 40.93
	ATOM	429 CG LEU 212	71.575 55.979 31.428 1.00 45.32
	ATOM	430 CD1 LEU 212	71.271 54.626 32.047 1.00 43.83
	ATOM	431 CD2 LEU 212	71.900 57.007 32.502 1.00 44.93
	ATOM	432 C LEU 212	72.448 55.050 28.133 1.00 37.61
25	ATOM	433 O LEU 212	71.318 54.805 27.719 1.00 33.71
	ATOM	434 N GLU 213	73.360 55.670 27.393 1.00 41.23
	ATOM	435 CA GLU 213	73.068 56.084 26.023 1.00 43.48
	ATOM	436 CB GLU 213	74.181 56.986 25.481 1.00 47.66
	ATOM	437 CG GLU 213	73.919 57.494 24.065 1.00 56.87
30	ATOM	438 CD GLU 213	75.121 58.180 23.433 1.00 60.87
	ATOM	439 OE1 GLU 213	76.258 57.996 23.924 1.00 60.37
	ATOM	440 OE2 GLU 213	74.921 58.894 22.423 1.00 61.13
	ATOM	441 C GLU 213	72.889 54.880 25.102 1.00 39.29
	ATOM	442 O GLU 213	71.965 54.841 24.290 1.00 36.66
35	ATOM	443 N ALA 214	73.785 53.906 25.233 1.00 36.33
	ATOM	444 CA ALA 214	73.739 52.693 24.422 1.00 34.89
	ATOM	445 CB ALA 214	74.946 51.817 24.711 1.00 30.70
	ATOM	446 C ALA 214	72.454 51.938 24.718 1.00 31.96
	ATOM	447 O ALA 214	71.739 51.523 23,804 1.00 33.93
40	ATOM	448 N PHE 215	72.151 51.798 26.003 1.00 28.47
	ATOM	449 CA PHE 215	70.947 51.116 26.445 1.00 29.74
	ATOM	450 CB PHE 215	70.819 51.223 27.962 1.00 23.73
	ATOM	451 CG PHE 215	69.589 50.568 28.515 1.00 22.71
	ATOM	452 CD1 PHE 215	69.603 49.220 28.858 1.00 22.53
45	ATOM	453 CD2 PHE 215	68.423 51.301 28.712 1.00 19.74
-	ATOM	454 CE1 PHE 215	68.477 48.606 29.391 1.00 20.75
	ATOM	455 CE2 PHE 215	67.290 50.698 29.245 1.00 21.02
	ATOM	456 CZ PHE 215	67.318 49.346 29.586 1.00 19.50
	ATOM	457 C PHE 215	69.730 51.742 25.771 1.00 34.64
50	ATOM	458 O PHE 215	68.872 51.034 25.239 1.00 39.86

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69.677 53.071 25.771 1.00 34.78
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                               68.572 53.801 25.160 1.00 36.01
            460 CA SER 216
    ATOM
                               68.762 55.302 25.366 1.00 37.36
    ATOM
            461 CB SER 216
                               67.537 55.987 25.193 1.00 48.33
            462 OG SER 216
    ATOM
            463 C SER 216
                              68.458 53.475 23.664 1.00 37.06
    ATOM
    ATOM
                              67.358 53.250 23.148 1.00 33.23
            464 O SER 216
                               69.601 53.410 22.986 1.00 36.25
            465 N GLU 217
    ATOM
            466 CA GLU 217
                                69.645 53.091 21.562 1.00 36.99
    ATOM
            467 CB GLU 217
                                71.092 53.104 21.064 1.00 37.10
    ATOM
                                71.682 54.491 20.912 1.00 44.30
            468 CG GLU 217
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    ATOM
            469 CD GLU 217
                                71.016 55.284 19.802 1.00 51.30
    ATOM
            470 OE1 GLU 217
                                71.439 55.142 18.633 1.00 57.25
    ATOM
                                70.070 56.046 20.096 1.00 52.50
            471 OE2 GLU 217
    ATOM
                               69.019 51.726 21.286 1.00 36.93
            472 C GLU 217
     ATOM
            473 O GLU 217
                               68.191 51.577 20.381 1.00 41.06
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     ATOM
            474 N PHE 218
                               69.395 50.740 22.093 1.00 30.27
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            475 CA PHE 218
                               68.875 49.388 21.947 1.00 27.20
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                               69.679 48.421 22.814 1.00 28.10
            476 CB PHE 218
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                                71.124 48.330 22.428 1.00 24.84
            477 CG PHE 218
     ATOM
                                72.117 48.286 23.398 1.00 21.78
            478 CD1 PHE 218
20
     ATOM
                                71.495 48.301 21.087 1.00 24.78
     ATOM
            479 CD2 PHE 218
            480 CE1 PHE 218
                                73.458 48.215 23.040 1.00 24.08
     ATOM
            481 CE2 PHE 218
                                72.834 48.230 20.719 1.00 25.33
     ATOM
                               73.818 48.187 21.697 1.00 25.04
     ATOM
            482 CZ PHE 218
            483 C PHE 218
                               67.381 49.281 22.261 1.00 28.23
25
     ATOM
            484 O PHE 218
                               66,639 48,605 21,543 1,00 33,52
     ATOM
                               66.927 49.961 23.310 1.00 27.24
            485 N THR 219
     ATOM
                                65.515 49.913 23.666 1.00 29.28
            486 CA THR 219
     ATOM
                                65.238 50.533 25.052 1.00 30.97
     ATOM 487 CB THR 219
                                65.724 51.880 25.090 1.00 35.50
            488 OG1 THR 219
30
     ATOM
                                65.901 49.712 26.149 1.00 30.78
            489 CG2 THR 219
     ATOM
            490 C THR 219
                               64.660 50.612 22.615 1.00 33.29
     ATOM
                               63.473 50.317 22.474 1.00 36.85
            491 O THR 219
     ATOM
                               65.276 51.515 21.860 1.00 35.23
            492 N LYS 220
     ATOM
                                64.579 52.253 20.816 1.00 38.97
            493 CA LYS 220
     ATOM
35
                                65.506 53.334 20.236 1.00 44.67
            494 CB LYS 220
     ATOM
                                64.805 54.491 19.513 1.00 58.02
            495 CG LYS 220
     ATOM
                                64.406 54.130 18.079 1.00 68.57
            496 CD LYS 220
     ATOM
                                63.732 55.296 17.347 1.00 70.50
     ATOM
            497 CE LYS 220
            498 NZ LYS 220
                                62.395 55.668 17.905 1.00 66.08
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     ATOM
                               64.112 51.289 19.721 1.00 38.48
            499 C LYS 220
     ATOM
                               63.021 51.446 19.173 1.00 37.18
             500 O LYS 220
     ATOM
                              64.917 50.270 19.432 1.00 36.19
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            501 N ILE 221
            502 CA ILE 221
                               64.563 49.305 18.394 1.00 36.77
     ATOM
                               65.756 48.996 17.457 1.00 34.41
             503 CB ILE 221
     ATOM
45
            504 CG2 ILE 221
                                66.270 50.276 16.814 1.00 38.54
     ATOM
                                66.864 48.267 18.221 1.00 32.93
            505 CG1 ILE 221
     ATOM
            506 CD1 ILE 221
                                67.984 47.752 17.338 1.00 31.12
     ATOM
                              64.002 47.971 18.888 1.00 38.22
            507 C ILE 221
     ATOM
                              63.499 47.181 18.089 1.00 38.90
            508 O ILE 221
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64.048 47.719 20.191 1.00 35.75
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    ATOM
    ATOM 511 CB ILE 222
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                              63.203 46.813 23.183 1.00 24.60
           512 CG2 ILE 222
    ATOM
                              64.147 44.638 22.350 1.00 32.60
    ATOM 513 CG1 ILE 222
    ATOM 514 CD1 ILE 222
                              64.860 44.226 23.609 1.00 34.52
                             62.042 46.240 20.624 1.00 32.56
    ATOM 515 C ILE 222
    ATOM 516 O ILE 222
                             61.581 45.109 20.452 1.00 35.74
                              61.262 47.313 20.720 1.00 29.43
    ATOM 517 N THR 223
    ATOM 518 CA THR 223
                               59.806 47.170 20.651 1.00 33.57
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    ATOM 519 CB THR 223
                               59.075 48.514 20.903 1.00 38.99
                               59.422 49.010 22.205 1.00 41.23
    ATOM 520 OG1 THR 223.
                               57.558 48.325 20.836 1.00 36.98
    ATOM 521 CG2 THR 223
    ATOM 522 C THR 223
                              59.355 46.528 19.325 1.00 31.45
                              58.571 45.571 19.334 1.00 26.77
    ATOM 523 O THR 223
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                              59.824 47.054 18.173 1.00 31.35
    ATOM 524 N PRO 224
    ATOM 525 CD PRO 224
                               60.570 48.306 17.950 1.00 30.11
    ATOM 526 CA PRO 224
                               59.424 46.462 16.891 1.00 30.38
    ATOM 527 CB PRO 224
                               60.149 47.336 15.865 1.00 30.09
    ATOM 528 CG PRO 224
                               60.200 48.659 16.530 1.00 31.86
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                              59.882 45.007 16.795 1.00 29.51
    ATOM 529 C PRO 224
                              59.147 44.153 16.295 1.00 32.52
    ATOM 530 O PRO 224
    ATOM 531 N ALA 225
                              61.090 44.734 17.285 1.00 22.63
    ATOM 532 CA ALA 225
                               61.650 43.385 17.268 1.00 20.88
                               63.046 43.386 17.862 1.00 20.57
    ATOM 533 CB ALA 225
25
                              60.752 42.416 18.026 1.00 23.53
    ATOM 534 C ALA 225
                              60.455 41.323 17.544 1.00 25.07
    ATOM 535 O ALA 225
    ATOM 536 N ILE 226
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    ATOM 537 CA ILE 226
                              59.120 42.644 21.360 1.00 20.25
    ATOM 538 CB ILE 226
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                               58.071 41.843 22.105 1.00 16.75
    ATOM 539 CG2 ILE 226
    ATOM 540 CG1 ILE 226
                               60.401 42.772 22.182 1.00 19.30
                               60.240 43.645 23.413 1.00 20.92
    ATOM 541 CD1 ILE 226
                             58.112 41.768 19.251 1.00 21.28
    ATOM 542 C ILE 226
                             57.553 40.670 19.256 1.00 23.75
    ATOM 543 O ILE 226
35
                              57.629 42.821 18.598 1.00 24.46
    ATOM 544 N THR 227
                               56.393 42.752 17.826 1.00 25.81
    ATOM 545 CA THR 227
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    ATOM 546 CB THR 227
                                55.772 45.039 18.345 1.00 35.43
    ATOM 547 OG1 THR 227
                                54,776 44.049 16.388 1.00 29.01
    ATOM 548 CG2 THR 227
                              56.508 41.728 16.691 1.00 22.85
    ATOM 549 C THR 227
                               55.589 40.939 16.469 1.00 22.84
    ATOM 550 O THR 227
                               57.647 41.713 16.004 1.00 16.09
     ATOM 551 N ARG 228
                               57.862 40.765 14.919 1.00 16.97
     ATOM 552 CA ARG 228
                               59.161 41.064 14.174 1.00 14.71
    ATOM 553 CB ARG 228
45
                               59.137 42.369 13.391 1.00 16.22
     ATOM 554 CG ARG 228
                               60.309 42.447 12.422 1.00 20.90
     ATOM 555 CD ARG 228
                               61.595 42.207 13.078 1.00 24.94
     ATOM 556 NE ARG 228
                               62.243 43.113 13.805 1.00 35.06
     ATOM 557 CZ ARG 228
                               61.729 44.328 13.973 1.00 36.35
     ATOM 558 NH1 ARG 228
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63.404 42.807 14.370 1.00 32.78
    ATOM 559 NH2 ARG 228
                              57.866 39.326 15.431 1.00 21.63
    ATOM 560 C ARG 228
    ATOM 561 O ARG 228
                              57.477 38.407 14.704 1.00 24.47
                              58,304 39.128 16.675 1.00 20.00
    ATOM 562 N VAL 229
                               58.319 37.793 17.266 1.00 18.39
    ATOM 563 CA VAL 229
                               59.103 37.745 18.606 1.00 19.20
    ATOM 564 CB VAL 229
                               58.938 36.382 19.265 1.00 14.19
    ATOM 565 CG1 VAL 229
                               60.581 38.001 18.356 1.00 14.81
    ATOM 566 CG2 VAL 229
    ATOM 567 C VAL 229
                              56.875 37.367 17.501 1.00 20.00
    ATOM 568 O VAL 229
                              56.499 36.227 17.212 1.00 20.04
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                              56.058 38.291 18.003 1.00 19.60
    ATOM 569 N VAL 230
                               54.651 37.996 18.247 1.00 18.72
    ATOM 570 CA VAL 230
    ATOM 571 CB VAL 230
                               53,930 39.185 18.912 1.00 22.15
    ATOM 572 CG1 VAL 230
                               52.452 38.862 19.113 1.00 15.66
                               54,592 39.522 20.248 1.00 21.05
    ATOM 573 CG2 VAL 230
15
                              53,967 37,660 16.917 1.00 26.17
    ATOM 574 C VAL 230
    ATOM 575 O VAL 230
                              53.188 36.704 16.836 1.00 28.01
    ATOM 576 N ASP 231
                              54.288 38.426 15.873 1.00 25.07
                               53.714 38.216 14.542 1.00 26.10
    ATOM 577 CA ASP 231
    ATOM 578 CB ASP 231
                               54.169 39.309 13.568 1.00 22.15
20
                               53.620 40.684 13.921 1.00 29.49
    ATOM 579 CG ASP 231
                               52.587 40.767 14.624 1.00 30.93
    ATOM 580 OD1 ASP 231
    ATOM 581 OD2 ASP 231
                               54.223 41.687 13.481 1.00 31.74
                              54.087 36.842 13.989 1.00 27.35
    ATOM 582 C ASP 231
                              53.245 36.154 13.408 1.00 25.89
    ATOM 583 O ASP 231
                              55.347 36.451 14.175 1.00 24.29
    ATOM 584 N PHE 232
    ATOM 585 CA PHE 232
                               55.825 35.154 13.714 1.00 22.90
                               57.302 34.956 14.090 1.00 20.56
    ATOM 586 CB PHE 232
                               57.762 33.525 14.007 1.00 24.20
    ATOM 587 CG PHE 232
                               57.952 32.910 12.772 1.00 23.44
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                               57.959 32.776 15.167 1.00 19.41
            589 CD2 PHE 232
    ATOM
    ATOM 590 CE1 PHE 232
                               58.329 31.567 12.689 1.00 19.53
                               58.336 31.431 15.100 1.00 21.09
    ATOM 591 CE2 PHE 232
    ATOM 592 CZ PHE 232
                               58.520 30.824 13.858 1.00 21.61
                              54.984 34.047 14.341 1.00 24.18
    ATOM 593 C PHE 232
35
                              54.481 33.160 13.645 1.00 22.26
    ATOM 594 O PHE 232
                              54.810 34.127 15.656 1.00 23.90
    ATOM 595 N ALA 233
                               54.048 33.128 16.397 1.00 22.60
    ATOM 596 CA ALA 233
                               54.088 33.435 17.890 1.00 15.34
    ATOM 597 CB ALA 233
                              52.609 33.040 15.917 1.00 22.04
    ATOM 598 C ALA 233
40
                               52.084 31.948 15.697 1.00 22.86
     ATOM 599 O ALA 233
                              51.978 34.195 15.743 1.00 25.04
           600 N LYS 234
     ATOM
                               50.593 34.248 15.298 1.00 27.68
     ATOM 601 CA LYS 234
     ATOM 602 CB LYS 234
                               50.096 35.691 15.292 1.00 31.41
     ATOM 603 CG LYS 234
                               49.845 36.248 16.682 1.00 40.37
45
                               49.212 37.626 16.604 1.00 57.53
     ATOM 604 CD LYS 234
                               48.772 38.112 17.974 1.00 64.28
     ATOM 605 CE LYS 234
                               48.164 39.473 17.904 1.00 67.19
     ATOM 606 NZ LYS 234
                              50.358 33.588 13.939 1.00 26.42
     ATOM 607 C LYS 234
   ATOM 608 O LYS 234
                              49.269 33.067 13.674 1.00 31.34
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	ATOM	609 N LYS 235	51.382 33.588 13.093 1.00 24.38
	ATOM	610 CA LYS 235	51.278 32.985 11.770 1.00 26.42
	ATOM	611 CB LYS 235	52.244 33.664 10.805 1.00 24.92
	ATOM	612 CG LYS 235	51.908 35.127 10.583 1.00 22.41
5	ATOM	613 CD LYS 235	52.843 35.775 9.588 1.00 29.38
	ATOM	614 CE LYS 235	52.481 37.234 9.395 1.00 33.49
	ATOM	615 NZ LYS 235	53.354 37.869 8.376 1.00 40.13
•	ATOM	616 C LYS 235	51.470 31.469 11.759 1.00 30.02
	ATOM	617 O LYS 235	51.417 30.838 10.699 1.00 30.37
10	ATOM	618 N LEU 236	51.722 30.889 12.930 1.00 32.39
	ATOM	619 CA LEU 236	51.878 29.443 13.053 1.00 36.24
	ATOM	620 CB LEU 236	52.944 29.080 14.089 1.00 29.91
	ATOM	621 CG LEU 236	54.373 29.516 13.765 1.00 24.69
	ATOM	622 CD1 LEU 236	55.299 29.054 14.877 1.00 22.71
15	ATOM	623 CD2 LEU 236	54.811 28.942 12.427 1.00 24.48
	ATOM	624 C LEU 236	50.520 28.891 13.470 1.00 41.22
	ATOM	625 O LEU 236	49.936 29.333 14.467 1.00 41.45
	ATOM	626 N PRO 237	50.012 27.895 12.729 1.00 47.86
	ATOM	627 CD PRO 237	50.739 27.190 11.657 1.00 49.32
20	ATOM	628 CA PRO 237	48.713 27.262 12.992 1.00 50.28
	ATOM	629 CB PRO 237	48.669 26.128 11.962 1.00 55.25
	ATOM	630 CG PRO 237	50.135 25.818 11.706 1.00 54.08
	ATOM	631 C PRO 237	48.495 26.751 14.422 1.00 47.94
	ATOM	632 O PRO 237	47.533 27.134 15.087 1.00 42.48
25	ATOM	633 N MET 238	49.415 25.927 14.906 1.00 49.51
	ATOM	634 CA MET 238	49.306 25.354 16.245 1.00 53.49
	ATOM	635 CB MET 238	50.379 24.275 16.424 1.00 52.52
	ATOM	636 CG MET 238	50.028 22.959 15.728 1.00 56.00
	ATOM	637 SD MET 238	51.443 21.961 15.204 1.00 50.16
30	ATOM	638 CE MET 238	50.896 21.440 13.552 1.00 55.71
	ATOM	639 C MET 238	49.352 26.362 17.395 1.00 54.20
	ATOM	640 O MET 238	48.930 26.058 18.515 1.00 54.72
	ATOM	641 N PHE 239	49.803 27.578 17.101 1.00 50.11
	ATOM	642 CA PHE 239	49.917 28.619 18.117 1.00 41.11
35 .	ATOM	643 CB PHE 239	51.089 29.552 17.788 1.00 34.80
	ATOM	644 CG PHE 239	51.336 30.607 18.826 1.00 30.25
	ATOM	645 CD1 PHE 239	52.127 30.332 19.937 1.00 25.66
	ATOM	646 CD2 PHE 239	50.786 31.878 18.690 1.00 26.30
	ATOM	647 CE1 PHE 239	52.368 31.307 20.896 1.00 30.28
40	ATOM	648 CE2 PHE 239	51.019 32.862 19.644 1.00 30.49
	ATOM	649 CZ PHE 239	51.813 32.576 20.750 1.00 29.00
	ATOM	650 C PHE 239	48.647 29.434 18.337 1.00 35.65
	ATOM	651 O PHE 239	48.151 29.521 19.457 1.00 30.27
	ATOM	652 N SER 240	48.133 30.037 17.272 1.00 36.49
45	ATOM	653 CA SER 240	46.936 30.866 17.359 1.00 36.37
	ATOM	654 CB SER 240	46.622 31.466 15.994 1.00 35.87
	ATOM	655 C SER 240	45.707 30.145 17.936 1.00 40.37
	ATOM	656 O SER 240	44.784 30.789 18.438 1.00 37.47
	ATOM	657 N GLU 241	45.713 28.814 17.889 1.00 43.00
50	ATOM	658 CA GLU 241	44.605 28.004 18.404 1.00 46.31

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                               44.750 26.422 16.360 1.00 69.03
            660 CG GLU 241
    ATOM
                               45.141 25.015 15.900 1.00 74.99
            661 CD GLU 241
    ATOM
    ATOM
                                45.835 24.299 16.658 1.00 77.81
            662 OE1 GLU 241
                                44.765 24.629 14.770 1.00 70.58
    ATOM
            663 OE2 GLU 241
                              44.587 27.961 19.933 1.00 42.60
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           664 C GLU 241
                               43.541 27.740 20.545 1.00 43.23
    ATOM 665 O GLU 241
                              45.762 28.125 20.535 1.00 39.31
    ATOM
            666 N LEU 242
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            667 CA LEU 242
    ATOM 668 CB LEU 242
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    ATOM
           669 CG LEU 242
                               48.311 26.974 21.853 1.00 27.59
                               49.750 27.307 22.180 1.00 20.72
            670 CD1 LEU 242
    ATOM
    ATOM 671 CD2 LEU 242
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           673 O LEU 242
                              44.956 30.282 22.119 1.00 31.50
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    ATOM
           674 N PRO 243
                              44.954 29.060 24.010 1.00 34.39
                               45.118 27.843 24.827 1.00 31.68
    ATOM 675 CD PRO 243
    ATOM
            676 CA PRO 243
                               44.309 30.134 24.773 1.00 34.39
            677 CB PRO 243
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    ATOM
                               44.081 28.026 25.892 1.00 33.80
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           678 CG PRO 243
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            679 C PRO 243
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    ATOM
                              46.517 31.082 24.897 1.00 34.99
            680 O PRO 243
    ATOM
                              44.791 32.532 24.946 1.00 34.23
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    ATOM 682 CA CYS 244
                               45.648 33.714 25.062 1.00 37.03
            683 CB CYS 244
                               44.820 34.960 25.376 1.00 43.49
25
    ATOM
                               43.820 35.531 24.007 1.00 71.28
            684 SG CYS 244
    ATOM
                              46.716 33.555 26.135 1.00 34.99
    ATOM
            685 C CYS 244
    ATOM
            686 O CYS 244
                              47.894 33.802 25.882 1.00 37.49
            687 N GLU 245
                               46.305 33.125 27.326 1.00 33.03
    ATOM
                               47.249 32.944 28.424 1.00 35.72
    ATOM
            688 CA GLU 245
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            689 CB GLU 245
                               46.559 32.469 29.716 1.00 37.85
    ATOM
                               45.294 31.633 29.549 1.00 46.81
    ATOM
           690 CG GLU 245
                               44.029 32.478 29.480 1.00 44.81
    ATOM
            691 CD GLU 245
                                43.606 33.012 30.527 1.00 33.05
    ATOM
            692 OE1 GLU 245
            693 OE2 GLU 245
                                43,454 32,599 28,377 1.00 48,22
    ATOM
35
                               48.414 32.035 28.047 1.00 32.29
            694 C GLU 245
    ATOM
                               49.558 32.319 28.399 1.00 35.92
    ATOM 695 O GLU 245
    ATOM 696 N ASP 246
                              48.134 30.975 27.295 1.00 30.64
                               49.182 30.058 26.855 1.00 28.23
    ATOM
            697 CA ASP 246
                               48,575 28.809 26.208 1.00 30.51
            698 CB ASP 246
     ATOM
                               48.213 27.737 27.222 1.00 33.18
     ATOM 699 CG ASP 246
                                48.265 28.006 28.439 1.00 31.26
     ATOM
            700 OD1 ASP 246
                                47.884 26.613 26.796 1.00 33.85
            701 OD2 ASP 246
     ATOM
                              50.104 30.757 25.860 1.00 30.10
     ATOM
            702 C ASP 246
45
     ATOM
            703 O ASP 246
                              51.330 30.651 25.950 1.00 27.08
                               49,500 31,477 24,918 1.00 30.39
            704 N GLN 247
     ATOM
                                50.249 32.208 23.901 1.00 29.08
            705 CA GLN 247
     ATOM
                               49.295 32.949 22.964 1.00 27.34
            706 CB GLN 247
     ATOM
                               48.390 32.034 22.147 1.00 28.95
     ATOM
            707 CG GLN 247
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     ATOM
            708 CD GLN 247
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47.850 33.918 20.767 1.00 33.23
    ATOM 709 OE1 GLN 247
    ATOM 710 NE2 GLN 247
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    ATOM 711 C GLN 247
                              52.377 33.261 24.256 1.00 28.70
    ATOM 712 O GLN 247
    ATOM 713 N ILE 248
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    ATOM 714 CA ILE 248
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                              50.525 35.662 27.303 1.00 28.96
    ATOM 715 CB ILE 248
                               51.356 36.476 28.279 1.00 28.67
    ATOM 716 CG2 ILE 248
    ATOM 717 CG1 ILE 248
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                              48.514 37.236 27.420 1.00 30.76
    ATOM 718 CD1 ILE 248
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                             52.618 34.259 27.006 1.00 28.39
    ATOM 719 C ILE 248
    ATOM 720 O ILE 248
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    ATOM 721 N ILE 249
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                             53.413 32.474 28.454 1.00 27.37
    ATOM 722 CA ILE 249
                              52.839 31.294 29.281 1.00 30.32
    ATOM 723 CB ILE 249
15
                               53.958 30.425 29.840 1.00 31.29
    ATOM 724 CG2 ILE 249
                               51.987 31.831 30.429 1.00 30.31
    ATOM 725 CG1 ILE 249
    ATOM 726 CD1 ILE 249
                               51.295 30.753 31.230 1.00 31.30
    ATOM 727 C ILE 249
                             54.510 31.974 27.509 1.00 28.63
                             55.701 32.100 27.808 1.00 29.59
    ATOM 728 O ILE 249
20
                              54.110 31.442 26.357 1.00 29.03
    ATOM 729 N LEU 250
                               55.068 30.934 25.380 1.00 22.44
    ATOM 730 CA LEU 250
                               54.351 30.166 24.266 1.00 24.30
    ATOM 731 CB LEU 250
                               53.665 28.866 24.687 1.00 23.20
    ATOM 732 CG LEU 250
                               52.951 28.273 23.502 1.00 20.36
    ATOM 733 CD1 LEU 250
25
    ATOM 734 CD2 LEU 250
                               54.685 27.880 25.238 1.00 19.45
    ATOM 735 C LEU 250
                              55.919 32.055 24.794 1.00 18.97
                              57.133 31.903 24.648 1.00 18.37
    ATOM 736 O LEU 250
                              55.291 33.180 24.468 1.00 20.63
    ATOM 737 N LEU 251
                               56.026 34.318 23.915 1.00 27.43
    ATOM 738 CA LEU 251
30
                               55.065 35.412 23.449 1.00 22.92
    ATOM 739 CB LEU 251
                               54.364 35.093 22.128 1.00 24.72
    ATOM
            740 CG LEU 251
                               53.342 36.167 21.821 1.00 32.13
            741 CD1 LEU 251
    ATOM
                               55.389 34.981 21.009 1.00 22.46
            742 CD2 LEU 251
    ATOM
                              57.026 34.875 24.930 1.00 27.23
35
    ATOM 743 C LEU 251
                              58.202 35.078 24.614 1.00 26.48
            744 O LEU 251
    ATOM
                              56.561 35.094 26.156 1.00 27.34
    ATOM 745 N LYS 252
    ATOM
            746 CA LYS 252
                               57.425 35.598 27.215 1.00 28.95
            747 CB LYS 252
                               56.649 35.715 28.527 1.00 32.89
    ATOM
                               55.570 36.783 28.530 1.00 35.06
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    ATOM
            748 CG LYS 252
    ATOM 749 CD LYS 252
                               55.084 37.028 29.943 1.00 42.82
    ATOM 750 CE LYS 252
                               54.124 38.191 30.003 1.00 53.05
                               53.677 38.451 31.398 1.00 64.03
    ATOM 751 NZ LYS 252
    ATOM 752 C LYS 252
                              58.605 34.647 27.405 1.00 27.66
                              59.734 35.076 27.646 1.00 33.16
45
            753 O LYS 252
    ATOM
                              58.344 33.357 27.243 1.00 24.50
    ATOM 754 N GLY 253
                               59.386 32.364 27.402 1.00 22.33
    ATOM 755 CA GLY 253
            756 C GLY 253
                              60.423 32.273 26.297 1.00 23.99
    ATOM
           757 O GLY 253
                              61.589 32.016 26.581 1.00 30.77
    ATOM
                              60.041 32.526 25.049 1.00 22.66
    ATOM 758 N CYS 254
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759 CA CYS 254
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    ATOM
                               60.386 31.494 22.868 1.00 24.86
    ATOM
            760 CB CYS 254
            761 SG CYS 254
                               58.996 32.276 22.014 1.00 25.55
    ATOM
            762 C CYS 254
                              61.399 33.702 23.242 1.00 23.79
    ATOM
            763 O CYS 254
                              62.262 33.685 22.357 1.00 22.18
    ATOM
            764 N CYS 255
                              60.788 34.814 23.625 1.00 19.49
    ATOM
            765 CA CYS 255
                               61.084 36.085 22.981 1.00 21.08
    ATOM
            766 CB CYS 255
                               60.336 37.220 23.669 1.00 18.21
    ATOM
    ATOM
            767 SG CYS 255
                               60.264 38.713 22.677 1.00 22.96
                              62.570 36.413 22.842 1.00 21.87
            768 C CYS 255
    ATOM
10
                              63.050 36.641 21.729 1.00 22.23
            769 O CYS 255
    ATOM
                               63.310 36.397 23.947 1.00 20.82
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            770 N MET 256
            771 CA MET 256
                               64.741 36.706 23.895 1.00 20.50
    ATOM
           772 CB MET 256
                               65.322 36.801 25.312 1.00 22.50
    ATOM
                               66.808 37.139 25.354 1.00 16.67
            773 CG MET 256
    ATOM
15
                               67.205 38.732 24.605 1.00 24.46
            774 SD MET 256
    ATOM
           775 CE MET 256
                               69.027 38.764 24.791 1.00 19.21
    ATOM
           776 C MET 256
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    ATOM
                               66.401 36.005 22.293 1.00 17.68
    ATOM
            777 O MET 256
            778 N GLU 257
                               65.149 34.404 23.248 1.00 20.33
    ATOM
20
            779 CA GLU 257
                               65.779 33.308 22.526 1.00 21.08
    ATOM
                               65.148 31.982 22.943 1.00 22.28
    ATOM
            780 CB GLU 257
    ATOM
            781 CG GLU 257
                               65.374 31.640 24.411 1.00 34.68
           782 CD GLU 257
                                64.515 30.486 24.907 1.00 43.20
    ATOM
                                63.823 29.836 24.091 1.00 42.14
           783 OE1 GLU 257
25
    ATOM
                                64.530 30.230 26.128 1.00 50.15
    ATOM
            784 OE2 GLU 257
            785 C GLU 257
                               65.650 33.503 21.018 1.00 19.26
    ATOM
           786 O GLU 257
                               66.632 33.360 20.276 1.00 18.09
    ATOM
                              64.446 33.850 20.566 1.00 16.30
            787 N ILE 258
    ATOM
           788 CA ILE 258
                              64.199 34.065 19.141 1.00 18.09
30
    ATOM
                              62.677 34.150 18.825 1.00 18.61
           789 CB ILE 258
    ATOM
            790 CG2 ILE 258
                               62.441 34.653 17.395 1.00 16.23
    ATOM
                               62.032 32.771 19.021 1.00 13.80
    ATOM
            791 CG1 ILE 258
            792 CD1 ILE 258
                               60.544 32.714 18.695 1.00 13.21
     ATOM
                              64.948 35.297 18.638 1.00 20.12
    ATOM 793 C ILE 258
35
                              65.605 35.242 17.593 1.00 19.17
     ATOM 794 O ILE 258
     ATOM 795 N MET 259
                               64.903 36.387 19.404 1.00 22.71
                                65.602 37.611 19.015 1.00 17.09
     ATOM
            796 CA MET 259
                                65.249 38.772 19.941 1.00 18.80
            797 CB MET 259
     ATOM
                                63.782 39.159 19.894 1.00 17.66
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     ATOM
            798 CG MET 259
            799 SD MET 259
                                63.457 40.748 20.678 1.00 25.77
     ATOM
            800 CE MET 259
                               63.774 40.377 22.374 1.00 16.65
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                               67.111 37.397 18.973 1.00 19.51
     ATOM 801 C MET 259
                               67.797 37.913 18.080 1.00 25.53
     ATOM
            802 O MET 259
            803 N SER 260
                               67.625 36.605 19.908 1.00 19.58
45
     ATOM
                               69.056 36.324 19.947 1.00 16.90
            804 CA SER 260
     ATOM
                               69,434 35.631 21.251 1.00 15.56
     ATOM
            805 CB SER 260
            806 OG SER 260
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     ATOM
            807 C SER 260
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     ATOM
                              70.496 35.761 18.129 1.00 22.82
     ATOM 808 O SER 260
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809 N LEU 261
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    ATOM
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    ATOM
            810 CA LEU 261
            811 CB LEU 261
                               67.878 32.552 17.092 1.00 18.38
    ATOM
                               67.890 31.708 15.812 1.00 14.47
            812 CG LEU 261
    ATOM
                                69.159 30.877 15.728 1.00 16.76
            813 CD1 LEU 261
    ATOM
                                66.672 30.806 15.793 1.00 14.06
    ATOM
            814 CD2 LEU 261
                              68.959 34.519 15.992 1.00 20.40
            815 C LEU 261
    ATOM
                              69.885 34.450 15.181 1.00 22.00
            816 O LEU 261
    ATOM
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    ATOM
            817 N ARG 262
            818 CA ARG 262
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    ATOM
                                66.530 37.067 14.782 1.00 20.29
            819 CB ARG 262
    ATOM
                                65.311 36.267 14.364 1.00 23.33
            820 CG ARG 262
    ATOM
           821 CD ARG 262
                                64.007 37.026 14.509 1.00 19.05
    ATOM
                                62.959 36.321 13.775 1.00 21.32
            822 NE ARG 262
    ATOM
                                61.780 36.837 13.441 1.00 23.44
            823 CZ ARG 262
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    ATOM
                                61.465 38.081 13.780 1.00 22.99
    ATOM 824 NH1 ARG 262
                                60.933 36.116 12.713 1.00 22.09
    ATOM 825 NH2 ARG 262
    ATOM
           826 C ARG 262
                               69.035 37.154 14.561 1.00 22.66
            827 O ARG 262
                               69.434 37.483 13.445 1.00 22.41
    ATOM
                               69.625 37.545 15.689 1.00 23.52
            828 N ALA 263
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           829 CA ALA 263
    ATOM
                               70.986 39.089 17.018 1.00 22.76
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            830 CB ALA 263
     ATOM 831 C ALA 263
                               72.052 37.530 15.366 1.00 22.85
     ATOM 832 O ALA 263
                               72.882 37.897 14.529 1.00 25.50
                               72.131 36.365 16.005 1.00 21.68
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           833 N ALA 264
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            834 CA ALA 264
     ATOM
                               73.092 34.256 16.763 1.00 15.97
     ATOM 835 CB ALA 264
     ATOM
            836 C ALA 264
                               73.401 34.957 14.382 1.00 23.11
                               74.523 34.831 13.892 1.00 24.87
            837 O ALA 264
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                               72.293 34.679 13.697 1.00 22.94
            838 N VAL 265
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            839 CA VAL 265
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                                71.072 33.547 11.797 1.00 25.97
     ATOM
            840 CB VAL 265
                                70.751 32.330 12.638 1.00 26.27
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            841 CG1 VAL 265
     ATOM
            842 CG2 VAL 265
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                               72.761 35.373 11.369 1.00 28.81
            843 C VAL 265
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                               72.966 35.160 10.176 1.00 31.92
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            844 O VAL 265
                               72.830 36.587 11.915 1.00 31.83
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                                73.210 37.774 11.150 1.00 33.19
            846 CA ARG 266
     ATOM
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                                72.141 38.861 11.258 1.00 31.67
            847 CB ARG 266
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            848 CG ARG 266
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                                69.913 39.668 10.454 1.00 33.95
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            849 CD ARG 266
                                68,955 39,532 9,361 1,00 38,15
            850 NE ARG 266
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                                67.688 39.927 9.410 1.00 37.39
            851 CZ ARG 266
     ATOM
                                67.198 40.491 10.509 1.00 29.92
            852 NH1 ARG 266
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                                66.918 39.770 8.340 1.00 31.24
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     ATOM
            853 NH2 ARG 266
                               74.565 38.307 11.604 1.00 36.31
            854 C ARG 266
     ATOM
                               74,821 39.516 11.575 1.00 38.56
     ATOM
            855 O ARG 266
                               75.416 37.393 12.056 1.00 34.21
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                               78.400 38.915 11.150 1.00 39.58
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                               79.170 40.511 9.434 1.00 44.38
            870 CB ASP 268
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                               80.145 40.770 8.290 1.00 50.31
     ATOM
            871 CG ASP 268
            872 OD1 ASP 268
                                80.290 39.901 7.400 1.00 55.79
     ATOM
                                80.773 41.847 8.280 1.00 50.24
            873 OD2 ASP 268
     ATOM
15
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                               81.305 39.645 11.208 1.00 42.75
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            876 N PRO 269
                                80.770 36.697 9.146 1.00 42.66
            877 CD PRO 269
     ATOM
            878 CA PRO 269
                                82.725 37.395 10.393 1.00 45.98
     ATOM
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                                81.631 35.506 9.458 1.00 43.33
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     ATOM
            881 C PRO 269
            882 O PRO 269
                               84.630 38.800 10.761 1.00 49.83
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            883 N ALA 270
                               83.486 39.100 8.840 1.00 53.62
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                                84.348 40.165 8.329 1.00 54.54
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                                83.892 40.585 6.929 1.00 51.24
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                               84.449 41.389 9.248 1.00 55.69
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            886 C ALA 270
            887. O ALA 270
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                               83.384 41.685 9.989 1.00 54.71
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                               83.378 42.838 10.889 1.00 51.26
            889 CA SER 271
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                               82.182 43.740 10.575 1.00 49.92
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                                82.065 43.976 9.183 1.00 60.09
            891 OG SER 271
     ATOM
            892 C SER 271
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                               83.482 43.288 13.240 1.00 52.11
            893 O SER 271
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                               83.051 41.162 12.619 1.00 48.96
            894 N ASP 272
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                                82.898 40.643 13.978 1.00 45.53
     ATOM
            895 CA ASP 272
            896 CB ASP 272
                                84.206 40.765 14.776 1.00 44.82
     ATOM
                                84.142 40.064 16.131 1.00 47.66
            897 CG ASP 272
     ATOM
                                84.750 40.581 17.091 1.00 48.64
             898 OD1 ASP 272
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     ATOM
            899 OD2 ASP 272
                                83.495 38.999 16.238 1.00 43.85
     ATOM
                               81.765 41.437 14.636 1.00 44.46
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             900 C ASP 272
                               81.904 41.958 15.747 1.00 42.41
             901 O ASP 272
     ATOM
                               80.652 41.551 13.915 1.00 39.79
             902 N THR 273
     ATOM
                                79.492 42.282 14.401 1.00 38.82
     ATOM 903 CA THR 273
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     ATOM 904 CB THR 273
                                79.334 43.648 13.670 1.00 39.73
                                 79.288 43.439 12.254 1.00 39.36
             905 OG1 THR 273
     ATOM
                                 80.496 44.578 13.991 1.00 41.31
             906 CG2 THR 273
     ATOM
                               78.203 41.485 14.211 1.00 38.36
             907 C THR 273
     ATOM
                               78.151 40.546 13.408 1.00 33.79
     ATOM 908 O THR 273
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77.187 41.835 14.995 1.00 36.91
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    ATOM 911 CB LEU 274
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    ATOM 912 CG LEU 274
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    ATOM 913 CD1 LEU 274
    ATOM 914 CD2 LEU 274
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    ATOM 915 C LEU 274
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    ATOM 918 CA THR 275
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                              72.824 42.674 11.542 1.00 35.14
    ATOM 919 CB THR 275
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    ATOM 920 OG1 THR 275
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    ATOM 921 CG2 THR 275
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    ATOM 922 C THR 275
                              71.100 41.670 13.845 1.00 36.53
    ATOM 923 O THR 275
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    ATOM 924 N LEU 276
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                              70.051 43.868 15.192 1.00 27.78
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    ATOM 926 CB LEU 276
                              70.205 44.780 16.420 1.00 22.51
                               71.383 44.532 17.373 1.00 25.89
    ATOM 927 CG LEU 276
                               71.225 45.408 18.608 1.00 20.70
    ATOM 928 CD1 LEU 276
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                               71.456 43.069 17.782 1.00 20.79
    ATOM 929 CD2 LEU 276
    ATOM 930 C LEU 276
                              68.930 44.376 14.296 1.00 27.27
    ATOM 931 O LEU 276.
                              69.068 45.430 13.672 1.00 29.06
                              67.854 43.598 14.187 1.00 25.97
    ATOM 932 N SER 277
                              66.697 43.957 13.366 1.00 28.63
    ATOM 933 CA SER 277
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    ATOM 934 CB SER 277
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                               65.561 44.905 15.290 1.00 22.65
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                              66.374 44.939 11.181 1.00 28.52
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                              68.168 43.597 11.465 1.00 31.24
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30
                              68.638 43.754 10.101 1.00 39.59
     ATOM 939 CA GLY 278
     ATOM 940 C GLY 278
                              68.999 45.178 9.706 1.00 44.55
     ATOM 941 O GLY 278
                              69.104 45.479 8.517 1.00 46.66
                              69.234 46.046 10.686 1.00 43.47
     ATOM 942 N GLU 279
                               69.566 47.435 10.387 1.00 43.87
     ATOM 943 CA GLU 279
35
                               68.314 48.312 10.515 1.00 44.28
     ATOM 944 CB GLU 279
                               67.703 48.322 11.908 1.00 52.30
     ATOM 945 CG GLU 279
     ATOM 946 CD GLU 279
                               66,440 49.159 12.001 1.00 60.23
                                66.398 50.074 12.853 1.00 63.06
     ATOM 947 OE1 GLU 279
     ATOM 948 OE2 GLU 279
                                65.485 48.894 11.238 1.00 65.67
40
                              70,700 48.038 11.216 1.00 42.40
     ATOM 949 C GLU 279
                               71.330 49.001 10.787 1.00 43.89
     ATOM 950 O GLU 279
                               70.977 47.472 12.388 1.00 40.86
     ATOM 951 N MET 280
                               72.027 48.009 13.248 1.00 32.80
     ATOM 952 CA MET 280
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     ATOM 953 CB MET 280
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     ATOM 955 SD MET 280
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    ATOM
                               76.519 46.727 12.023 1.00 34.42
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                              76.125 46.950 14.482 1.00 36.76
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                              76.416 48.129 14.693 1.00 34.59
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    ATOM 968 CG2 VAL 282
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    ATOM 975 CD LYS 283
                               83.092 47.416 16.618 1.00 59.26
    ATOM 976 CE LYS 283
                              83.481 47.813 15.202 1.00 62.52
                              82.492 48.742 14.588 1.00 66.27
    ATOM 977 NZ LYS 283
                              80.075 44.746 19.559 1.00 38.78
    ATOM 978 C LYS 283
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                              79.283 45.257 20.356 1.00 40.63
    ATOM
           979 O LYS 283
    ATOM 980 N ARG 284
                              80.900 43.753 19.881 1.00 36.01
                               80.908 43.104 21.189 1.00 38.62
    ATOM 981 CA ARG 284
                               82.150 42.224 21.327 1.00 38.83
    ATOM 982 CB ARG 284
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    ATOM 983 CG ARG 284
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            984 CD ARG 284
                               83.506 39.120 19.644 1.00 45.18
            985 NE ARG 284
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                               83.259 37.905 20.128 1.00 44.79
            986 CZ ARG 284
    ATOM
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    ATOM 987 NH1 ARG 284
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    ATOM 988 NH2 ARG 284
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    ATOM 989 C ARG 284
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           991 N GLU 285
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    ATOM
                               81.724 46.002 23.525 1.00 37.18
    ATOM 992 CA GLU 285
                               82.950 46.906 23.422 1.00 36.65
    ATOM 993 CB GLU 285
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    ATOM 994 C GLU 285
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                              79.921 47.074 24.704 1.00 33.00
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                               78.714 48.061 22.425 1.00 32.31
     ATOM 997 CA GLN 286
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                               78.440 48.525 20.997 1.00 38.24
40
                               79.565 49.352 20.392 1.00 42.42
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     ATOM 1000 CD GLN 286
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                                79.103 48.910 18.089 1.00 42.21
     ATOM 1001 OE1 GLN 286
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     ATOM 1002 NE2 GLN 286
                               77.484 47.355 23.002 1.00 33.08
     ATOM 1003 C GLN 286
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     ATOM 1004 O GLN 286
                               77.245 46.114 22.579 1.00 31.49
     ATOM 1005 N LEU 287
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     ATOM 1006 CA LEU 287
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     ATOM 1008 CG LEU 287
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	ATOM	1010 CD2 LEU 287	73.393 44.205 22.616 1.00 14.41
	ATOM	1011 C LEU 287	76.298 44.986 24.538 1.00 32.80
	ATOM	1012 O LEU 287	75.351 45.014 25.334 1.00 32.10
5	ATOM	1013 N LYS 288	77.536 44.641 24.885 1.00 32.54
	ATOM	1014 CA LYS 288	77.897 44.280 26.251 1.00 30.70
	ATOM	1015 CB LYS 288	79.376 43.893 26.315 1.00 31.24
	ATOM	1016 CG LYS 288	79.834 43.382 27.662 1.00 34.69
	ATOM	1017 CD LYS 288	81.227 42.784 27.574 1.00 37.69
10	ATOM	1018 CE LYS 288	81.638 42.177 28.904 1.00 42.86
	ATOM	1019 NZ LYS 288	82.883 41.369 28.786 1.00 49.63
	ATOM	1020 C LYS 288	77.611 45.448 27.189 1.00 28.74
	ATOM	1021 O LYS 288	76.827 45.319 28.129 1.00 34.45
	ATOM	1022 N ASN 289	78.190 46.602 26.882 1.00 26.57
15	ATOM	1023 CA ASN 289	78.011 47.803 27.691 1.00 30.84
	ATOM	1024 CB ASN 289	79.012 48.879 27.274 1.00 26.04
	ATOM	1025 CG ASN 289	80.437 48.485 27.570 1.00 35.16
	ATOM	1026 OD1 ASN 289	80.700 47.718 28.499 1.00 42.54
	ATOM	1027 ND2 ASN 289	81.371 48.998 26.784 1.00 32.82
20	ATOM	1028 C ASN 289	76.602 48.371 27.620 1.00 35.05
	ATOM	1029 O ASN 289	76.154 49.039 28.550 1.00 36.94
	ATOM	1030 N GLY 290	75.909 48.113 26.515 1.00 32.43
	ATOM	1031 CA GLY 290	74.556 48.614 26.345 1.00 28.66
	ATOM	1032 C GLY 290	73.525 48.024 27.289 1.00 28.48
25	ATOM	1033 O GLY 290	72.377 48.467 27.308 1.00 28.17
	ATOM	1034 N GLY 291	73.908 47.002 28.047 1.00 28.66
	ATOM	1035 CA GLY 291	72.969 46.408 28.980 1.00 29.19
	ATOM	1036 C GLY 291	72.976 44.894 29.075 1.00 29.76 72.595 44.340 30.105 1.00 34.44
20	ATOM	1037 O GLY 291 1038 N LEU 292	73.399 44.213 28.017 1.00 29.69
30	ATOM	1038 N LEU 292 1039 CA LEU 292	73.410 42.755 28.036 1.00 30.64
	ATOM ATOM	1039 CA LEU 292 1040 CB LEU 292	73.421 42.194 26.611 1.00 27.07
	ATOM	1040 CB LEU 292	72.113 42.348 25.833 1.00 23.27
	ATOM	1041 CG LEG 292	72.202 41.580 24.532 1.00 22.24
35	ATOM	1042 CD1 LEU 292	70.950 41.827 26.661 1.00 23.80
33	ATOM	1044 C LEU 292	74.530 42.125 28.861 1.00 29.22
	ATOM	1045 O LEU 292	74.365 41.033 29.404 1.00 31.02
	ATOM	1046 N GLY 293	75.671 42.800 28.945 1.00 30.26
	ATOM	1047 CA GLY 293	76.788 42.259 29.700 1.00 28.37
40	ATOM	1048 C GLY 293	77.307 40.995 29.040 1.00 29.85
	ATOM	1049 O GLY 293	77.460 40.951 27.820 1.00 32.37
	ATOM	1050 N VAL 294	77.537 39.953 29.832 1.00 30.08
	ATOM	1051 CA VAL 294	78.041 38.687 29.308 1.00 31.62
	ATOM	1052 CB VAL 294	78.466 37.716 30.442 1.00 29.11
45	ATOM	1053 CG1 VAL 294	79.649 38.292 31.191 1.00 31.37
	ATOM	1054 CG2 VAL 294	77.304 37.443 31.396 1.00 26.69
	ATOM	1055 C VAL 294	77.079 37.978 28.351 1.00 32.81
	ATOM	1056 O VAL 294	77.496 37.095 27.591 1.00 33.00
	ATOM	1057 N VAL 295	75.801 38.356 28.380 1.00 30.45
50	ATOM	1058 CA VAL 295	74.814 37.752 27.487 1.00 28.02

	ATOM	1059 CB VAL 295	73.378 38.232 27.793 1.00 29.96
	ATOM	1060 CG1 VAL 295	72.380 37.575 26.838 1.00 22.55
	ATOM	1061 CG2 VAL 295	73.016 37.903 29.232 1.00 20.10
	ATOM	1062 C VAL 295	75.203 38.115 26.057 1.00 29.90
5	ATOM	1063 O VAL 295	75.047 37.312 25.140 1.00 34.47
	ATOM	1064 N SER 296	75.762 39.309 25.886 1.00 29.11
	ATOM	1065 CA SER 296	76.215 39.771 24.581 1.00 30.96
	ATOM	1066 CB SER 296	76.785 41.184 24.702 1.00 27.26
	ATOM	1067 OG SER 296	77.300 41.648 23.469 1.00 22.93
10	ATOM	1068 C SER 296	77.294 38.811 24.080 1.00 36.41
	ATOM	1069 O SER 296	77.238 38.341 22.939 1.00 38.84
	ATOM	1070 N ASP 297	78.254 38.501 24.954 1.00 35.29
	ATOM	1071 CA ASP 297	79.346 37.585 24.629 1.00 32.14
	ATOM	1072 CB ASP 297	80.245 37.356 25.851 1.00 36.57
15	ATOM	1073 CG ASP 297	80.958 38.616 26.307 1.00 41.75
	ATOM	1074 OD1 ASP 297	81.492 39.352 25.447 1.00 45.45
	ATOM	1075 OD2 ASP 297	80.999 38.861 27.532 1.00 45.15
	ATOM	1076 C ASP 297	78.768 36.249 24.191 1.00 29.61
	ATOM	1077 O ASP 297	79.242 35.644 23.231 1.00 32.90
20	ATOM	1078 N ALA 298	77.738 35.804 24.903 1.00 27.85
	ATOM	1079 CA ALA 298	77.071 34.544 24.608 1.00 27.89
	ATOM	1080 CB ALA 298	75.998 34.258 25.657 1.00 21.67
	ATOM	1081 C ALA 298	76.462 34.539 23.202 1.00 28.26
	ATOM	1082 O ALA 298	76.648 33.579 22.446 1.00 30.19
25	ATOM	1083 N ILE 299	75.744 35.606 22.853 1.00 25.20
	ATOM	1084 CA ILE 299	75.119 35.708 21.537 1.00 23.46
	ATOM	1085 CB ILE 299	74.200 36.944 21.427 1.00 21.63
	ATOM	1086 CG2 ILE 299	73.491 36.946 20.078 1.00 22.20
	ATOM	1087 CG1 ILE 299	73.145 36.914 22.536 1.00 19.79
30	ATOM	1088 CD1 ILE 299	72.245 38.139 22.578 1.00 18.33
	ATOM	1089 C ILE 299	76.181 35.752 20.444 1.00 26.28
	ATOM	1090 O ILE 299	76.043 35.095 19.414 1.00 31.72
	ATOM	1091 N PHE 300	77.247 36.512 20.675 1.00 29.35
	ATOM	1092 CA PHE 300	78.338 36.613 19.709 1.00 29.01
35	ATOM	1093 CB PHE 300	79.386 37.622 20.182 1.00 29.53
	ATOM	1094 CG PHE 300	79.239 38.978 19.562 1.00 27.60
	ATOM	1095 CD1 PHE 300	78.481 39.964 20.179 1.00 24.86
	ATOM	1096 CD2 PHE 300	79.853 39.266 18.350 1.00 27.39
	ATOM	1097 CE1 PHE 300	78.337 41.218 19.597 1.00 25.66
40	ATOM	1098 CE2 PHE 300	79.715 40.518 17.761 1.00 25.97
	ATOM	1099 CZ PHE 300	78.956 41.495 18.384 1.00 21.03
	ATOM	1100 C PHE 300	78.988 35.248 19.496 1.00 30.34
	ATOM	1101 O PHE 300	79.309 34.873 18.367 1.00 29.35
	ATOM	1102 N GLU 301	79.181 34.507 20.582 1.00 31.04
45	ATOM	1103 CA GLU 301	79.775 33.178 20.499 1.00 33.60
	ATOM	1104 CB GLU 301	80.012 32.607 21.898 1.00 31.64
	ATOM	1105 C GLU 301	78.851 32.265 19.696 1.00 33.90
	ATOM	1106 O GLU 301	79.315 31.473 18.872 1.00 33.33
	ATOM	1107 N LEU 302	
50	ATOM	1108 CA LEU 302	76.556 31.581 19.227 1.00 27.57

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	ATOM ATOM ATOM	1109 CB LEU 302 1110 CG LEU 302 1111 CD1 LEU 302	75.150 31.842 19.776 1.00 25.24 73.994 31.131 19.059 1.00 28.59 74.066 29.634 19.299 1.00 25.52
	ATOM	1112 CD2 LEU 302	72.660 31.682 19.532 1.00 19.30
5	ATOM	1113 C LEU 302	76.601 31.904 17.739 1.00 26.80
	ATOM	1114 O LEU 302	76.682 31.003 16.904 1.00 27.81
	ATOM	1115 N GLY 303	76.576 33.195 17.416 1.00 26.47
	ATOM	1116 CA GLY 303	76.611 33.624 16.030 1.00 26.99
	ATOM	1117 C GLY 303	77.845 33.133 15.295 1.00 33.46
10	ATOM	1118 O GLY 303	77.757 32.646 14.164 1.00 32.33
	ATOM	1119 N LYS 304	78.994 33.232 15.956 1.00 34.63 80.269 32.813 15.383 1.00 36.20
	ATOM	1120 CA LYS 304	81.399 33.115 16.372 1.00 41.96
	ATOM	1121 CB LYS 304 1122 CG LYS 304	82.779 33.179 15.757 1.00 47.05
15	ATOM ATOM	1122 CG LYS 304 1123 CD LYS 304	83.800 33.610 16.796 1.00 59.47
15	ATOM	1124 CE LYS 304	85.179 33.791 16.181 1.00 65.89
	ATOM	1124 CE E13 304 1125 NZ LYS 304	85.182 34.863 15.144 1.00 71.01
	ATOM	1126 C LYS 304	80.276 31.332 14.992 1.00 33.17
	ATOM	1127 O LYS 304	80.752 30.974 13.913 1.00 34.44
20	ATOM	1128 N SER 305	79.739 30.482 15.861 1.00 31.40
	ATOM	1129 CA SER 305	79.687 29.048 15.594 1.00 33.10
	ATOM	1130 CB SER 305	79.513 28.266 16.900 1.00 34.10
	ATOM	1131 OG SER 305	78.391 28.727 17.633 1.00 40.61
	ATOM	1132 C SER 305	78.597 28.664 14.589 1.00 33.02
25	ATOM	1133 O SER 305	78.771 27.718 13.816 1.00 35.32
	ATOM	1134 N LEU 306	77.488 29.404 14.580 1.00 32.14
	ATOM	1135 CA LEU 306	76.391 29.121 13.653 1.00 31.02
	ATOM	1136 CB LEU 306	75.138 29.936 13.996 1.00 22.76
	ATOM	1137 CG LEU 306	74.361 29.487 15.235 1.00 24.42
30	ATOM	1138 CD1 LEU 306	73.094 30.311 15.380 1.00 23.13 74.016 28.009 15.126 1.00 25.53
	ATOM	1139 CD2 LEU 306 1140 C LEU 306	74.016 28.009 13.126 1.00 23.33 76.780 29.354 12.198 1.00 33.11
	ATOM	-	76.161 28.796 11.293 1.00 32.60
	ATOM ATOM	1141 O LEU 306 1142 N SER 307	77.821 30.153 11.975 1.00 36.12
35	ATOM	1142 N SER 307 1143 CA SER 307	78.296 30.448 10.624 1.00 38.80
33	ATOM	1144 CB SER 307	79.514 31.373 10.677 1.00 41.64
	ATOM	1145 OG SER 307	79.224 32.556 11.401 1.00 54.66
	ATOM	1146 C SER 307	78.650 29.182 9.845 1.00 36.98
	ATOM	1147 O SER 307	78.302 29.055 8.669 1.00 42.87
40	ATOM	1148 N ALA 308	79.315 28.239 10.509 1.00 35.72
	ATOM	1149 CA ALA 308	79.719 26.983 9.879 1.00 32.70
	ATOM	1150 CB ALA 308	80.683 26.227 10.782 1.00 33.88
	ATOM	1151 C ALA 308	78.531 26.093 9.521 1.00 34.83
	ATOM	1152 O ALA 308	78.620 25.278 8.600 1.00 39.61
45	ATOM	1153 N PHE 309	77.424 26.250 10.244 1.00 31.54
	ATOM	1154 CA PHE 309	76.226 25.453 9.999 1.00 32.43
	ATOM	1155 CB PHE 309	75.259 25.558 11.182 1.00 30.89
	ATOM	1156 CG PHE 309	75.718 24.826 12.415 1.00 33.73
	ATOM		76.769 25.314 13.183 1.00 40.48
50	ATOM	1158 CD2 PHE 309	75.091 23.654 12.816 1.00 35.96

	ATOM	1159 CE1 PHE 309	77.189 24.643 14.334 1.00 37.87
	ATOM	1160 CE2 PHE 309	75.502 22.975 13.962 1.00 38.44
	ATOM	1161 CZ PHE 309	76.553 23.471 14.722 1.00 37.34
	ATOM	1162 C PHE 309	75.507 25.809 8.693 1.00 34.76
5	ATOM	1163 O PHE 309	74.810 24.969 8.118 1.00 36.18
	ATOM	1164 N ASN 310	75.693 27.040 8.218 1.00 35.80
	ATOM	1165 CA ASN 310	75.060 27.506 6.980 1.00 41.00
	ATOM	1166 CB ASN 310	75.705 26.852 5.755 1.00 51.94
	ATOM	1167 CG ASN 310	77.053 27.452 5.419 1.00 67.92
10	ATOM	1168 OD1 ASN 310	77.139 28.439 4.687 1.00 77.32
	ATOM	1169 ND2 ASN 310	78.116 26.869 5.962 1.00 72.62
	ATOM	1170 C ASN 310	73.560 27.245 6.985 1.00 38.15
	ATOM	1171 O ASN 310	73.034 26.515 6.141 1.00 35.87
	ATOM	1172 N LEU 311	72.885 27.819 7.971 1.00 33.94
15	ATOM		71.450 27.651 8.111 1.00 32.09
	ATOM	1174 CB LEU 311	71.011 28.009 9.533 1.00 28.06
	ATOM	1175 CG LEU 311	71.656 27.301 10.724 1.00 26.38
	ATOM	1176 CD1 LEU 311	71.092 27.883 12.012 1.00 23.56
	ATOM	1177 CD2 LEU 311	71.409 25.801 10.651 1.00 21.24
20	ATOM	1178 C LEU 311	70.705 28.542 7.124 1.00 33.00
	ATOM	1179 O LEU 311	71.173 29.630 6.782 1.00 35.47
	ATOM	1180 N ASP 312	69.569 28.057 6.638 1.00 27.78
	ATOM	1181 CA ASP 312	68.749 28.841 5.733 1.00 27.06
0.5	ATOM	1182 CB ASP 312	68.385 28.049 4.456 1.00 25.84
25	ATOM	1183 CG ASP 312	67.580 26.778 4.724 1.00 25.67 67.124 26.541 5.860 1.00 28.20
	ATOM		67.124 26.341 3.860 1.00 28.20 67.387 26.008 3.762 1.00 27.62
	ATOM	-	67.517 29.314 6.514 1.00 28.51
	ATOM	1186 C ASP 312 1187 O ASP 312	67.371 28.990 7.703 1.00 25.35
30	ATOM ATOM	1188 N ASP 313	66.633 30.060 5.855 1.00 22.16
30	ATOM	1189 CA ASP 313	65.430 30.589 6.494 1.00 21.37
	ATOM	1190 CB ASP 313	64.625 31.431 5.499 1.00 25.11
	ATOM	1191 CG ASP 313	65.380 32.666 5.025 1.00 31.54
	ATOM		65.119 33.115 3.890 1.00 35.35
35	ATOM	1193 OD2 ASP 313	66.225 33.193 5.783 1.00 35.37
,,	ATOM	1194 C ASP 313	64.524 29.535 7.120 1.00 21.11
	ATOM	1195 O ASP 313	63.904 29.783 8.158 1.00 23.68
		1196 N THR 314	64.440 28.367 6.489 1.00 22.88
	ATOM	1197 CA THR 314	63.591 27.281 6.981 1.00 22.81
40	ATOM	1198 CB THR 314	63.472 26.155 5.927 1.00 26.00
	ATOM	1199 OG1 THR 314	62.873 26.679 4.732 1.00 20.14
	ATOM	1200 CG2 THR 314	62.629 25.010 6.457 1.00 17.51
	ATOM	1201 C THR 314	64.086 26.706 8.310 1.00 19.46
	ATOM	1202 O THR 314	63.312 26.529 9.247 1.00 19.33
45	ATOM	1203 N GLU 315	65.381 26.431 8.392 1.00 17.49
	ATOM	1204 CA GLU 315	65.965 25.885 9.611 1.00 20.62
	ATOM	1205 CB GLU 315	67.426 25.514 9.358 1.00 14.39
	ATOM	1206 CG GLU 315	67.539 24.339 8.400 1.00 13.07
	ATOM	1207 CD GLU 315	68.923 24.125 7.835 1.00 14.98
50	ATOM	1208 OE1 GLU 315	69.634 25.116 7.552 1.00 17.71

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ATOM 1209 OE2 GLU 315
                                69.287 22.948 7.651 1.00 17.88
                               65.810 26.883 10.762 1.00 20.57
    ATOM 1210 C GLU 315
                               65.368 26.518 11.854 1.00 18.43
    ATOM 1211 O GLU 315
                               66.096 28.154 10.488 1.00 19.19
    ATOM 1212 N VAL 316
                                65.955 29.203 11.490 1.00 16.53
    ATOM 1213 CA VAL 316
                                66.418 30.567 10.933 1.00 17.42
    ATOM 1214 CB VAL 316
                                66.149 31.687 11.940 1.00 13.89
    ATOM 1215 CG1 VAL 316
                                67.900 30.506 10.594 1.00 14.31
    ATOM 1216 CG2 VAL 316
    ATOM 1217 C VAL 316
                               64.488 29.291 11.927 1.00 19.53
                               64.191 29.448 13.110 1.00 19.86
    ATOM 1218 O VAL 316
10
                               63.575 29.159 10.970 1.00 19.02
    ATOM 1219 N ALA 317
                                62.145 29.215 11.254 1.00 16.95
    ATOM 1220 CA ALA 317
                                61.357 29.239 9.951 1.00 17.68
    ATOM 1221 CB ALA 317
    ATOM 1222 C ALA 317
                               61.674 28.047 12.126 1.00 14.13
                               60.875 28.228 13.045 1.00 15.34
    ATOM 1223 O ALA 317
15
                               62.154 26.847 11.819 1.00 17.41
    ATOM 1224 N LEU 318
    ATOM 1225 CA LEU 318
                                61.769 25.653 12.569 1.00 19.10
                               62.186 24.398 11.802 1.00 18.21
    ATOM 1226 CB LEU 318
                                61.443 24.209 10.473 1.00 19.02
    ATOM 1227 CG LEU 318
                                62.105 23.128 9.646 1.00 16.10
     ATOM 1228 CD1 LEU 318
20
                                59.987 23.875 10.735 1.00 11.32
    ATOM 1229 CD2 LEU 318
                               62.399 25.685 13.954 1.00 22.38
    ATOM 1230 C LEU 318
     ATOM 1231 O LEU 318
                               61.782 25.278 14.945 1.00 21.64
     ATOM 1232 N LEU 319
                               63.619 26.207 14.016 1.00 20.97
                               64.338 26.344 15.270 1.00 19.71
25
     ATOM 1233 CA LEU 319
                                65.715 26.951 15.005 1.00 20.56
     ATOM 1234 CB LEU 319
     ATOM 1235 CG LEU 319
                                66.722 27.036 16.152 1.00 32.05
                                66.704 25.760 16.963 1.00 33.15
     ATOM 1236 CD1 LEU 319
                                68.109 27.303 15.590 1.00 28.25
     ATOM 1237 CD2 LEU 319
                               63.496 27.254 16.164 1.00 20.66
     ATOM 1238 C LEU 319
30
                               63.215 26.920 17.313 1.00 24.47
     ATOM 1239 O LEU 319
                               63.026 28.365 15.604 1.00 19.25
     ATOM 1240 N GLN 320
     ATOM 1241 CA GLN 320
                                62.191 29.307 16.346 1.00 19.02
                                61.842 30.526 15.488 1.00 19.11
     ATOM 1242 CB GLN 320
                                63.032 31.377 15.101 1.00 20.02
35
     ATOM 1243 CG GLN 320
                                62.665 32.562 14.224 1.00 23.65
     ATOM 1244 CD GLN 320
                                63.487 33.445 13.997 1.00 22.68
     ATOM 1245 OE1 GLN 320
                                61.440 32.574 13.704 1.00 20.77
     ATOM 1246 NE2 GLN 320
                               60,905 28.635 16.811 1.00 20.52
     ATOM 1247 C GLN 320
     ATOM 1248 O GLN 320
                               60.465 28.845 17.938 1.00 22.04
40
                               60.306 27.825 15.942 1.00 21.01
     ATOM 1249 N ALA 321
                                59.069 27.128 16.280 1.00 16.83
     ATOM 1250 CA ALA 321
                                58.556 26.358 15.079 1.00 16.58
     ATOM 1251 CB ALA 321
                               59.288 26.185 17.462 1.00 18.15
     ATOM 1252 C ALA 321
                               58.427 26.069 18.344 1.00 13.03
     ATOM 1253 O ALA 321
45
                               60.442 25.523 17.481 1.00 14.89
     ATOM 1254 N VAL 322
     ATOM 1255 CA VAL 322
                                60.774 24.599 18.559 1.00 19.05
                                62.051 23.779 18.233 1.00 21.50
     ATOM 1256 CB VAL 322
     ATOM 1257 CG1 VAL 322
                                62.510 22.990 19.457 1.00 21.49
                               61.773 22.819 17.073 1.00 15.42
     ATOM 1258 CG2 VAL 322
50
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	ATOM ATOM	1259 C VAL 322 1260 O VAL 322	60.947 25.375 19.867 1.00 19.89 60.478 24.940 20.919 1.00 21.58
	ATOM	1261 N LEU 323	61.591 26.537 19.788 1.00 20.25
	ATOM	1262 CA LEU 323	61.804 27.387 20.959 1.00 19.32
5	ATOM	1263 CB LEU 323	62.683 28.586 20.597 1.00 12.95
J	ATOM	1264 CG LEU 323	64.129 28.273 20.217 1.00 20.70
	ATOM	1265 CD1 LEU 323	64.805 29.503 19.641 1.00 13.23
	ATOM	1266 CD2 LEU 323	64.883 27.767 21.438 1.00 22.91
	ATOM	1267 C LEU 323	60.468 27.884 21.497 1.00 20.25
10	ATOM	1268 O LEU 323	60.251 27.918 22.706 1.00 25.88
••	ATOM	1269 N LEU 324	59.571 28.251 20.587 1.00 23.08
	ATOM	1270 CA LEU 324	58.248 28.753 20.944 1.00 21.24
	ATOM	1271 CB LEU 324	57.555 29.333 19.707 1.00 18.45
	ATOM	1272 CG LEU 324	56.119 29.847 19.868 1.00 17.07
15	ATOM	1273 CD1 LEU 324	56.083 31.092 20.752 1.00 15.39
	ATOM	1274 CD2 LEU 324	55.545 30.162 18.498 1.00 17.90
	ATOM	1275 C LEU 324	57.342 27.706 21.598 1.00 21.54
	ATOM	1276 O LEU 324	56.742 27.967 22.642 1.00 23.41
	ATOM	1277 N MET 325	57.249 26.521 21.003 1.00 24.63
20	ATOM	1278 CA MET 325	56.380 25.476 21.545 1.00 25.35
	ATOM	1279 CB MET 325	55.901 24.536 20.430 1.00 25.53
	ATOM	1280 CG MET 325	55.235 25.220 19.232 1.00 21.89
	ATOM	1281 SD MET 325	53.871 26.337 19.649 1.00 25.50
	ATOM	1282 CE MET 325	52.705 25.250 20.397 1.00 17.66
25	ATOM	1283 C MET 325	57.031 24.676 22.675 1.00 27.58
	ATOM	1284 O MET 325	56.988 23.450 22.690 1.00 28.61
	ATOM	1285 N SER 326	57.613 25.376 23.638 1.00 27.98
	ATOM	1286 CA SER 326	58.265 24.718 24.757 1.00 31.60
	ATOM	1287 CB SER 326	59.527 25.493 25.155 1.00 35.80
30	ATOM	1288 OG SER 326	60.123 24.966 26.327 1.00 43.74
	ATOM	1289 C SER 326	57.313 24.624 25.939 1.00 32.12
	ATOM	1290 O SER 326	56.590 25.574 26.240 1.00 30.91
	ATOM	1291 N THR 327	57.276 23.464 26.583 1.00 35.41
	ATOM	1292 CA THR 327	56.420 23.278 27.747 1.00 39.61
35	ATOM	1293 CB THR 327	55.777 21.890 27.758 1.00 38.84
	ATOM		56.784 20.890 27.538 1.00 42.53
	ATOM	1295 CG2 THR 327	54.716 21.802 26.679 1.00 40.78
	ATOM	1296 C THR 327	
40	ATOM	1297 O THR 327	
40	ATOM	1298 N ASP 328	59.309 24.308 29.987 1.00 47.33
	ATOM	1299 CA ASP 328 1300 CB ASP 328	60.750 24.358 29.482 1.00 58.03
	ATOM		61.718 23.687 30.425 1.00 72.16
	ATOM	1301 CG ASP 328 1302 OD1 ASP 328	61.816 24.117 31.595 1.00 82.32
15	ATOM	1302 OD1 ASP 328	62.378 22.720 29.994 1.00 81.63
45	ATOM ATOM	1303 OD2 ASP 328	58.951 25.625 30.676 1.00 47.99
	ATOM		59.830 26.373 31.093 1.00 53.33
	ATOM		57.657 25.910 30.780 1.00 48.33
	ATOM	1307 CA ARG 329	57.177 27.135 31.413 1.00 47.67
50	ATOM		
50	AIOM	1500 CD AICO 329	JU.JUL 20.071 JU.J/7 1.00 17.01

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57.550 28.802 29.450 1.00 47.87
    ATOM 1309 CG ARG 329
    ATOM 1310 CD ARG 329
                                57.893 27.968 28.226 1.00 44.00
    ATOM 1311 NE ARG 329
                                58.759 28.682 27.288 1.00 41.17
                                60.087 28.605 27.283 1.00 48.58
    ATOM 1312 CZ ARG 329
                                60.719 27.848 28.172 1.00 52.94
    ATOM 1313 NH1 ARG 329
 5
    ATOM 1314 NH2 ARG 329
                                60.784 29.257 26.362 1.00 43.16
                               56.126 26.778 32.457 1.00 48.01
    ATOM 1315 C ARG 329
                               55.573 25.677 32.437 1.00 50.22
    ATOM 1316 O ARG 329
    ATOM 1317 N SER 330
                               55.832 27.716 33.351 1.00 47.37
                               54.848 27.490 34.402 1.00 47.64
    ATOM 1318 CA SER 330
10
    ATOM 1319 CB SER 330
                               55,376 28,021 35,736 1.00 46.62
                              53.506 28.139 34.074 1.00 46.40
    ATOM 1320 C SER 330
                               53.460 29.252 33.548 1.00 48.49
    ATOM 1321 O SER 330
                               52.421 27.424 34.359 1.00 44.16
    ATOM 1322 N GLY 331
                               51.090 27.956 34.123 1.00 41.44
    ATOM 1323 CA GLY 331
15
    ATOM 1324 C GLY 331
                               50.424 27.660 32.790 1.00 42.83
    ATOM 1325 O GLY 331
                               49.478 28.351 32.413 1.00 45.88
    ATOM 1326 N LEU 332
                               50.889 26.643 32.075 1.00 40.10
                               50.288 26.300 30.789 1.00 39.27
    ATOM 1327 CA LEU 332
                               51.301 25.596 29.885 1.00 37.42
    ATOM 1328 CB LEU 332
20
                                52.436 26.426 29.291 1.00 35.35
    ATOM 1329 CG LEU 332
                                53.374 25.505 28.530 1.00 31.61
    ATOM 1330 CD1 LEU 332
    ATOM 1331 CD2 LEU 332
                                51.875 27.511 28.376 1.00 31.82
                               49.058 25.415 30.951 1.00 39.32
    ATOM 1332 C LEU 332
                               49.060 24.467 31.738 1.00 42.74
    ATOM 1333 O LEU 332
25
                               48.009 25.730 30.202 1.00 37.62
    ATOM 1334 N LEU 333
                               46.778 24.953 30.241 1.00 41.30
     ATOM 1335 CA LEU 333
     ATOM 1336 CB LEU 333
                               45.586 25.835 29.852 1.00 43.52
                                45.125 26.904 30.848 1.00 49.39
     ATOM 1337 CG LEU 333
                                44,296 27.970 30.142 1.00 46.19
     ATOM 1338 CD1 LEU 333
30
                                44.330 26.248 31.968 1.00 51.29
     ATOM 1339 CD2 LEU 333
                               46.859 23.762 29.285 1.00 41.39
     ATOM 1340 C LEU 333
                               46.565 22.628 29.657 1.00 43.41
     ATOM 1341 O LEU 333
                               47.317 24.024 28.067 1.00 42.18
     ATOM 1342 N CYA 334
                                47.409 23.003 27.029 1.00 39.56
     ATOM 1343 CA CYA 334
35
                                47.004 23.616 25.691 1.00 45.48
     ATOM 1344 CB CYA 334
                                45.517 24.616 25.785 1.00 51.57
     ATOM 1345 SG CYA 334
                                44.187 22.808 25.555 1.00 90.90
     ATOM 1346 AS CYA 334
                               48.776 22.347 26.891 1.00 38.28
     ATOM 1347 C CYA 334
     ATOM 1348 O CYA 334
                               49.273 22.178 25.778 1.00 40.95
40
     ATOM 1349 N VAL 335
                               49.345 21.913 28.009 1.00 36.05
                                50.661 21.278 28.006 1.00 35.78
     ATOM 1350 CA VAL 335
                                50.996 20.679 29.399 1.00 35.53
     ATOM 1351 CB VAL 335
                                52.413 20.123 29.407 1.00 32.76
     ATOM 1352 CG1 VAL 335
     ATOM 1353 CG2 VAL 335
                                50.822 21.729 30.490 1.00 28.87
45
                               50.776 20.170 26.950 1.00 36.41
     ATOM 1354 C VAL 335
                               51.756 20.104 26.202 1.00 34.26
     ATOM 1355 O VAL 335
     ATOM 1356 N ASP 336
                               49.756 19.323 26.880 1.00 38.42
                               49.736 18.209 25.942 1.00 39.71
     ATOM 1357 CA ASP 336
                               48.485 17.359 26.179 1.00 51.53
     ATOM 1358 CB ASP 336
50
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ATOM 1359 CG ASP 336
                               48.534 16.028 25.452 1.00 65.98
                                49.240 15.114 25.934 1.00 70.75
    ATOM 1360 OD1 ASP 336
    ATOM 1361 OD2 ASP 336
                                47.858 15.891 24.406 1.00 72.15
                              49.794 18.668 24.486 1.00 37.72
    ATOM 1362 C ASP 336
                              .50.686 18.259 23.733 1.00 32.08
    ATOM 1363 O ASP 336
                               48.858 19.532 24.100 1.00 33.78
    ATOM 1364 N LYS 337
                               48.797 20.040 22.731 1.00 28.00
    ATOM 1365 CA LYS 337
                               47.626 21.022 22.574 1.00 22.46
    ATOM 1366 CB LYS 337
                              50.116 20.704 22.334 1.00 29.06
    ATOM 1367 C LYS 337
                              50.607 20.512 21.220 1.00 28.41
    ATOM 1368 O LYS 337
10
                              50.705 21.449 23.267 1.00 27.56
    ATOM 1369 N ILE 338
                               51.964 22.138 23.022 1.00 25.03
    ATOM 1370 CA ILE 338
    ATOM 1371 CB ILE 338
                               52.274 23.149 24.144 1.00 19.49
                               53.577 23.876 23.859 1.00 19.00
    ATOM 1372 CG2 ILE 338
                               51.135 24.167 24.232 1.00 21.97
    ATOM 1373 CG1 ILE 338
15
                               51.277 25.175 25.348 1.00 26.67
    ATOM 1374 CD1 ILE 338
                              53.119 21.153 22.826 1.00 29.97
    ATOM 1375 C ILE 338
    ATOM 1376 O ILE 338
                              53.935 21.328 21.914 1.00 31.00
                               53.165 20.100 23.642 1.00 33.52
    ATOM 1377 N GLU 339
                                54.213 19.080 23.516 1.00 35.34
    ATOM 1378 CA GLU 339
20
                                54.136 18.062 24.659 1.00 39.97
    ATOM 1379 CB GLU 339
    ATOM 1380 CG GLU 339
                                54.653 18.585 25.986 1.00 53.23
                                54.549 17.579 27.126 1.00 61.16
    ATOM 1381 CD GLU 339
                                53.602 16.759 27.131 1.00 64.30
    ATOM 1382 OE1 GLU 339
                                55.412 17.622 28.031 1.00 57.76
    ATOM 1383 OE2 GLU 339
25
                               54.091 18.353 22.178 1.00 31.63
    ATOM 1384 C GLU 339
                               55.086 18.123 21.491 1.00 28.96
    ATOM 1385 O GLU 339
    ATOM 1386 N LYS 340
                               52.861 18.006 21.810 1.00 30.95
                              52.602 17.313 20.554 1.00 31.58
    ATOM 1387 CA LYS 340
                               51.121 16.966 20.438 1.00 31.83
    ATOM 1388 CB LYS 340
30
                               53.057 18.159 19.358 1.00 29.84
    ATOM 1389 C LYS 340
    ATOM 1390 O LYS 340
                               53.696 17.640 18.438 1.00 31.58
                               52.765 19.460 19.388 1.00 25.33
     ATOM 1391 N SER 341
                               53.165 20.351 18.297 1.00 23.92
     ATOM 1392 CA SER 341
                               52.468 21.707 18.400 1.00 24.02
    ATOM 1393 CB SER 341
35
                                52,700 22,302 19,657 1,00 48,88
     ATOM 1394 OG SER 341
                               54.677 20.533 18.240, 1.00 24.39
     ATOM 1395 C SER 341
                               55.254 20.593 17.150 1.00 24.71
     ATOM 1396 O SER 341
                               55.324 20.606 19.405 1.00 25.45
     ATOM 1397 N GLN 342
                                56,777 20.751 19.437 1.00 26.66
     ATOM 1398 CA GLN 342
40
     ATOM 1399 CB GLN 342
                                57.311 20.975 20.853 1.00 22.77
                                58.805 21.307 20.840 1.00 25.76
     ATOM 1400 CG GLN 342
                                59.427 21.371 22.214 1.00 28.46
     ATOM 1401 CD GLN 342
                                59.342 20.422 22.990 1.00 34.22
     ATOM 1402 OE1 GLN 342
                                 60.080 22.483 22.517 1.00 30.01
     ATOM 1403 NE2 GLN 342
45
                               57.425 19.504 18.843 1.00 23.37
     ATOM 1404 C GLN 342
                               58.414 19.598 18.106 1.00 23.65
     ATOM 1405 O GLN 342
                               56.864 18.340 19.162 1.00 21.48
     ATOM 1406 N GLU 343
                               57.370 17.076 18.641 1.00 20.74
     ATOM 1407 CA GLU 343
                                56.599 15.902 19.247 1.00 22.09
     ATOM 1408 CB GLU 343
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57.225 17.094 17.119 1.00 19.18
    ATOM 1409 C GLU 343
                               58.156 16.743 16.393 1.00 21.11
    ATOM 1410 O GLU 343
                               56.077 17.570 16.648 1.00 19.93
    ATOM 1411 N ALA 344
                                55.803 17.662 15.217 1.00 20.20
    ATOM 1412 CA ALA 344
                               54.411 18.216 14.989 1.00 16.46
    ATOM 1413 CB ALA 344
    ATOM 1414 C ALA 344
                               56.850 18.539 14.528 1.00 20.75
    ATOM 1415 O ALA 344
                               57.432 18.140 13.514 1.00 25.13
    ATOM 1416 N TYR 345
                               57.105 19.722 15.088 1.00 21.31
    ATOM 1417 CA TYR 345
                               58.107 20.631 14.531 1.00 15.93
                               58.127 21.969 15.282 1.00 17.29
    ATOM 1418 CB TYR 345
10
                                57.049 22.927 14.833 1.00 16.11
    ATOM 1419 CG TYR 345
                                56.017 23.296 15.689 1.00 9.93
    ATOM 1420 CD1 TYR 345
    ATOM 1421 CE1 TYR 345
                                54.999 24.138 15.263 1.00 16.95
                                57.041 23.431 13.531 1.00 19.84
    ATOM 1422 CD2 TYR 345
                                56.026 24.276 13.094 1.00 17.13
    ATOM 1423 CE2 TYR 345
15
                               55.005 24.622 13.963 1.00 18.12
    ATOM 1424 CZ TYR 345
    ATOM 1425 OH TYR 345
                                53.980 25.430 13.530 1.00 26.25
                               59.493 20.008 14.554 1.00 20.65
    ATOM 1426 C TYR 345
                               60.240 20.129 13.583 1.00 20.75
    ATOM 1427 O TYR 345
                               59.832 19.337 15.655 1.00 22.14
    ATOM 1428 N LEU 346
20
                               61.134 18.684 15.803 1.00 19.43
    ATOM 1429 CA LEU 346
                               61.267 18.041 17.186 1.00 19.92
    ATOM 1430 CB LEU 346
    ATOM 1431 CG LEU 346
                                61.683 18.945 18.347 1.00 25.56
                                61.440 18.244 19.677 1.00 22.06
    ATOM 1432 CD1 LEU 346
                                63.147 19.332 18.197 1.00 17.62
    ATOM 1433 CD2 LEU 346
25
                               61.359 17.635 14.723 1.00 19.30
    ATOM 1434 C LEU 346
    ATOM 1435 O LEU 346
                               62.441 17.560 14.142 1.00 22.84
                               60.337 16.826 14.456 1.00 25.17
    ATOM 1436 N LEU 347
                                60.423 15.790 13.427 1.00 24.55
    ATOM 1437 CA LEU 347
                                59.187 14.892 13.453 1.00 25.47
    ATOM 1438 CB LEU 347
30
                                59.256 13.654 14.345 1.00 30.65
    ATOM 1439 CG LEU 347
                                57.941 12.890 14.258 1.00 34.28
     ATOM 1440 CD1 LEU 347
     ATOM 1441 CD2 LEU 347
                                60.416 12.765 13.908 1.00 28.26
                               60.584 16.400 12.042 1.00 24.00
     ATOM 1442 C LEU 347
                               61.399 15.932 11.245 1.00 29.74
     ATOM 1443 O LEU 347
35
                               59.809 17.443 11.761 1.00 22.72
     ATOM 1444 N ALA 348
                                59.875 18.125 10.475 1.00 19.19
     ATOM 1445 CA ALA 348
                                58.789 19.188 10.388 1.00 22.73
     ATOM 1446 CB ALA 348
                               61.246 18.762 10.316 1.00 20.34
     ATOM 1447 C ALA 348
                               61.881 18.633 9.274 1.00 23.94
     ATOM 1448 O ALA 348
40
     ATOM 1449 N PHE 349
                               61.707 19.402 11.388 1.00 22.19
                                63.001 20.078 11.435 1.00 19.41
     ATOM 1450 CA PHE 349
                                63.185 20.701 12.832 1.00 17.45
     ATOM 1451 CB PHE 349
                                64,371 21.632 12.963 1.00 18.70
     ATOM 1452 CG PHE 349
                                65.183 21.943 11.874 1.00 19.09
     ATOM 1453 CD1 PHE 349
45
                                64.669 22.203 14.199 1.00 21.81
     ATOM 1454 CD2 PHE 349
                                66.270 22.811 12.012 1.00 21.49
     ATOM 1455 CE1 PHE 349
                                65.753 23.072 14.351 1.00 18.58
     ATOM 1456 CE2 PHE 349
     ATOM 1457 CZ PHE 349
                                66.555 23.376 13.256 1.00 18.67
                               64.110 19.071 11.136 1.00 20.96
     ATOM 1458 C PHE 349
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64.967 19.311 10.283 1.00 25.19
    ATOM 1459 O PHE 349
                               64.076 17.935 11.824 1.00 23.96
    ATOM 1460 N GLU 350
                               65.077 16.888 11.642 1.00 27.98
    ATOM 1461 CA GLU 350
                               64.794 15.721 12.591 1.00 28.90
    ATOM 1462 CB GLU 350
                               65.738 14.542 12.413 1.00 39.36
    ATOM 1463 CG GLU 350
                               65.603 13.497 13.505 1.00 41.62
    ATOM 1464 CD GLU 350
                                64.475 13.260 13.988 1.00 43.67
    ATOM 1465 OE1 GLU 350
                                66.636 12.908 13.876 1.00 49.64
    ATOM 1466 OE2 GLU 350
                               65.100 16.385 10.203 1.00 27.12
    ATOM 1467 C GLU 350
    ATOM 1468 O GLU 350
                               66.158 16.288 9.577 1.00 27.44
10
                              63.918 16.088 9.678 1.00 27.36
    ATOM 1469 N HIS 351
                               63.787 15.591 8.318 1.00 23.97
    ATOM 1470 CA HIS 351
    ATOM 1471 CB HIS 351
                               62.366 15.087 8.090 1.00 22.89
                               61.991 13.945 8.986 1.00 24.58
    ATOM 1472 CG HIS 351
                               62.736 13.209 9.846 1.00 25.83
    ATOM 1473 CD2 HIS 351
15
                               60.709 13.448 9.073 1.00 26.50
    ATOM 1474 ND1 HIS 351
                               60.677 12.460 9.948 1.00 24.81
    ATOM 1475 CE1 HIS 351
                               61.896 12.295 10.431 1.00 28.42
    ATOM 1476 NE2 HIS 351
                              64.200 16.635 7.278 1.00 24.22
    ATOM 1477 C HIS 351
                              64.757 16.287 6.236 1.00 25.79
    ATOM 1478 O HIS 351
20
                               63.969 17.912 7.572 1.00 21.04
    ATOM 1479 N TYR 352
                               64.363 18.974 6.654 1.00 18.98
    ATOM 1480 CA TYR 352
                               63.770 20.321 7.067 1.00 17.08
    ATOM 1481 CB TYR 352
    ATOM 1482 CG TYR 352
                                64.127 21.413 6.090 1.00 21.83
                                63.537 21.467 4.828 1.00 20.07
    ATOM 1483 CD1 TYR 352
25
                                63.941 22.411 3.883 1.00 23.51
    ATOM 1484 CE1 TYR 352
    ATOM 1485 CD2 TYR 352
                                65.121 22.339 6.388 1.00 19.94
                                65.531 23.284 5.452 1.00 20.85
    ATOM 1486 CE2 TYR 352
                               64.942 23.313 4.203 1.00 24.80
    ATOM 1487 CZ TYR 352
                                65.380 24.221 3.269 1.00 26.74
    ATOM 1488 OH TYR 352
30
                               65.889 19.055 6.624 1.00 20.58
    ATOM 1489 C TYR 352
    ATOM 1490 O TYR 352
                               66.492 19.276 5.570 1.00 22.72
                               66.508 18.877 7.789 1.00 28.34
    ATOM 1491 N VAL 353
                                67.967 18.892 7.904 1.00 22.38
     ATOM 1492 CA VAL 353
                                68.419 18.755 9.389 1.00 26.46
    ATOM 1493 CB VAL 353
35
                                69.915 18.527 9.478 1.00 20.92
     ATOM 1494 CG1 VAL 353
                                68.053 20.009 10.165 1.00 22.46
     ATOM 1495 CG2 VAL 353
                               68.518 17.725 7.078 1.00 23.51
     ATOM 1496 C VAL 353
                               69.535 17.865 6.391 1.00 24.73
     ATOM 1497 O VAL 353
                               67.850 16.575 7.158 1.00 20.93
40
     ATOM 1498 N ASN 354
     ATOM 1499 CA ASN 354
                                68.252 15.392 6.397 1.00 27.25
                                67.320 14.210 6.680 1.00 28.43
    ATOM 1500 CB ASN 354
                                67.521 13.607 8.058 1.00 31.50
     ATOM 1501 CG ASN 354
                                68,565 13.787 8.692 1.00 37.79
     ATOM 1502 OD1 ASN 354
                                66.521 12.867 8.524 1.00 26.44
     ATOM 1503 ND2 ASN 354
45
                               68.182 15.721 4.908 1.00 31.27
     ATOM 1504 C ASN 354
                               69.066 15.347 4.134 1.00 34.22
     ATOM 1505 O ASN 354
                              67.124 16.429 4.520 1.00 30.49
     ATOM 1506 N HIS 355
                               66.917 16.826 3.132 1.00 26.88
     ATOM 1507 CA HIS 355
                               65.548 17.494 2.975 1.00 27.27
     ATOM 1508 CB HIS 355
50
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65.319 18.103 1.625 1.00 37.76
    ATOM 1509 CG HIS 355
                               65.439 19.382 1.196 1.00 35.28
    ATOM 1510 CD2 HIS 355
                               64.913 17.369 0.532 1.00 34.93
    ATOM 1511 ND1 HIS 355
                               64.789 18.169 -0.513 1.00 34.84
    ATOM 1512 CE1 HIS 355
                               65.104 19.394 -0.135 1.00 33.13
    ATOM 1513 NE2 HIS 355
                              68.016 17.748 2.610 1.00 24.66
    ATOM 1514 C HIS 355
                              68.420 17.630 1.456 1.00 26.62
    ATOM 1515 O HIS 355
                               68.487 18.670 3.448 1.00 25.86
    ATOM 1516 N ARG 356
                                69.536 19.608 3.040 1.00 26.94
    ATOM 1517 CA ARG 356
                                69.620 20.791 3.996 1.00 20.57
    ATOM 1518 CB ARG 356
10
                                68.453 21.727 3.899 1.00 19.69
    ATOM 1519 CG ARG 356
                                68.866 23.110 4.340 1.00 23.81
    ATOM 1520 CD ARG 356
                                69.768 23.746 3.388 1.00 23.14
    ATOM 1521 NE ARG 356
                                70.641 24.697 3.702 1.00 24.11
    ATOM 1522 CZ ARG 356
                                70.755 25.129 4.949 1.00 26.29
    ATOM 1523 NH1 ARG 356
15
                                71.384 25.242 2.754 1.00 32.79
    ATOM 1524 NH2 ARG 356
                               70.921 19.002 2.875 1.00 29.38
    ATOM 1525 C ARG 356
                               71.795 19.607 2.257 1.00 32.91
    ATOM 1526 O ARG 356
                               71.133 17.848 3.498 1.00 33.39
    ATOM 1527 N LYS 357
                               72.401 17.128 3.417 1.00 35.97
    ATOM 1528 CA LYS 357
20
                               72.479 16.363 2.089 1.00 40.55
    ATOM 1529 CB LYS 357
                                71.327 15.381 1.891 1.00 44.03
    ATOM 1530 CG LYS 357
    ATOM 1531 CD LYS 357
                                71.360 14.722 0.523 1.00 52.31
                               70.171 13.787 0.343 1.00 56.99
    ATOM 1532 CE LYS 357
                               70.208 13.085 -0.970 1.00 64.78
     ATOM 1533 NZ LYS 357
25
                               73.657 17.981 3.629 1.00 38.55
     ATOM 1534 C LYS 357
                               74.518 18.079 2.748 1.00 42.50
     ATOM 1535 O LYS 357
                              73.751 18.601 4.802 1.00 35.00
     ATOM 1536 N HIS 358
                               74.906 19.418 5.155 1.00 32.94
     ATOM 1537 CA HIS 358
                               74.732 20.018 6.552 1.00 27.62
     ATOM 1538 CB HIS 358
30
                               73.669 21.067 6.643 1.00 26.64
     ATOM 1539 CG HIS 358
                               72.330 20.968 6.819 1.00 20.85
     ATOM 1540 CD2 HIS 358
                                73.950 22.416 6.587 1.00 24.71
     ATOM 1541 ND1 HIS 358
                               72.831 23.103 6.724 1.00 21.02
     ATOM 1542 CE1 HIS 358
                                71.834 22.248 6.865 1.00 21.42
     ATOM 1543 NE2 HIS 358
35
                              76.140 18.520 5.176 1.00 36.60
     ATOM 1544 C HIS 358
                               76.072 17.379 5.635 1.00 38.73
     ATOM 1545 O HIS 358
                               77.267 19.037 4.702 1.00 41.40
     ATOM 1546 N ASN 359
                                78.515 18.277 4.689 1.00 45.02
     ATOM 1547 CA ASN 359
                                79.441 18.799 3.587 1.00 42.57
     ATOM 1548 CB ASN 359
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     ATOM 1549 C ASN 359
                               79.193 18.386 6.058 1.00 46.59
     ATOM 1550 O ASN 359
                               80.405 18.588 6.150 1.00 52.31
                               78.400 18.254 7.117 1.00 45.14
     ATOM 1551 N ILE 360
                               78.896 18.348 8.487 1.00 43.69
     ATOM 1552 CA ILE 360
     ATOM 1553 CB ILE 360
                               78.330 19.597 9.207 1.00 40.08
45
                                78.824 19.657 10.645 1.00 32.11
     ATOM 1554 CG2 ILE 360
                                78.733 20.864 8.452 1.00 41.47
     ATOM 1555 CG1 ILE 360
                                78.057 22.115 8.954 1.00 44.93
     ATOM 1556 CD1 ILE 360
                              78,452 17.101 9.242 1.00 43.63
     ATOM 1557 C ILE 360
                               77.257 16.797 9.313 1.00 45.20
     ATOM 1558 O ILE 360
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ATOM 1559 N PRO 361
                               79.413 16.337 9.780 1.00 43.91
                                80.871 16.540 9.699 1.00 47.07
    ATOM 1560 CD PRO 361
                                79.087 15.118 10.526 1.00 41.66
    ATOM 1561 CA PRO 361
                                80.462 14.495 10.782 1.00 43.73
    ATOM 1562 CB PRO 361
                                81.383 15.679 10.830 1.00 45.45
    ATOM 1563 CG PRO 361
    ATOM 1564 C PRO 361
                               78.332 15.403 11.832 1.00 36.42
                               78.679 16.325 12.572 1.00 35.74
    ATOM 1565 O PRO 361
                              77.291 14.610 12.088 1.00 33.14
    ATOM 1566 N HIS 362
                               76.462 14.726 13.292 1.00 34.09
    ATOM 1567 CA HIS 362
    ATOM 1568 CB HIS 362
                               77.288 14.413 14.547 1.00 33.82
10
                               78.132 13.181 14.424 1.00 36.04
    ATOM 1569 CG HIS 362
                               77.793 11.885 14.224 1.00 34.77
    ATOM 1570 CD2 HIS 362
    ATOM 1571 ND1 HIS 362
                                79.509 13.212 14.482 1.00 37.16
                               79.983 11.990 14.325 1.00 37.16
    ATOM 1572 CE1 HIS 362
    ATOM 1573 NE2 HIS 362
                               78.962 11.165 14.167 1.00 40.13
15
                              75.829 16.110 13.417 1.00 31.00
     ATOM 1574 C HIS 362
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     ATOM 1575 O HIS 362
    ATOM 1576 N PHE 363
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     ATOM 1577 CA PHE 363
                                74.878 18.021 12.200 1.00 28.08
                                74.503 18.355 10.747 1.00 25.26
    ATOM 1578 CB PHE 363
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                                73.923 19.733 10.567 1.00 24.91
     ATOM 1579 CG PHE 363
                                74.750 20.817 10.320 1.00 27.60
     ATOM 1580 CD1 PHE 363
     ATOM 1581 CD2 PHE 363
                                72.552 19.948 10.664 1.00 25.52
     ATOM 1582 CE1 PHE 363
                                74.221 22.100 10.175 1.00 29.70
                                72.014 21.227 10.522 1.00 25.88
25
    ATOM 1583 CE2 PHE 363
                                72.850 22.304 10.278 1.00 21.49
     ATOM 1584 CZ PHE 363
                               73.659 18.201 13.099 1.00 23.79
     ATOM 1585 C PHE 363
     ATOM 1586 O PHE 363
                               73.587 19.164 13.863 1.00 24.48
                               72.707 17.277 13.012 1.00 23.13
     ATOM 1587 N TRP 364
                               71.484 17.369 13.805 1.00 25.06
     ATOM 1588 CA TRP 364
30
                                70.536 16.201 13.494 1.00 21.17
     ATOM 1589 CB TRP 364
                                69.247 16.220 14.271 1.00 23.14
     ATOM 1590 CG TRP 364
                                68.261 17.266 14.296 1.00 27.68
     ATOM 1591 CD2 TRP 364
     ATOM 1592 CE2 TRP 364
                                67.229 16.845 15.165 1.00 28.31
                                68.149 18.517 13.671 1.00 26.46
     ATOM 1593 CE3 TRP
                          364
35
                                68.784 15.241 15.096 1.00 23.76
     ATOM 1594 CD1 TRP 364
     ATOM 1595 NE1 TRP 364
                                67.576 15.607 15.637 1.00 32.12
                                66.100 17.628 15.427 1.00 25.63
     ATOM 1596 CZ2 TRP
                          364
     ATOM 1597 CZ3 TRP 364
                                67.028 19.294 13.931 1.00 25.55
                                66.017 18.845 14.803 1.00 29.79
     ATOM 1598 CH2 TRP 364
                               71.715 17.531 15.312 1.00 27.80
     ATOM 1599 C TRP 364
                               71.212 18.486 15.904 1.00 26.96
     ATOM 1600 O TRP 364
                               72.458 16.605 15.955 1.00 30.69
     ATOM 1601 N PRO 365
                                72.974 15.308 15.481 1.00 31.45
     ATOM 1602 CD PRO 365
                                72.687 16.757 17.397 1.00 27.97
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     ATOM 1603 CA PRO 365
     ATOM 1604 CB PRO 365
                                73.506 15.512 17.752 1.00 26.50
                                73.057 14.509 16.757 1.00 33.47
     ATOM 1605 CG PRO 365
                               73.457 18.043 17.709 1.00 27.10
     ATOM 1606 C PRO 365
                               73.154 18.736 18.681 1.00 26.88
     ATOM 1607 O PRO 365
     ATOM 1608 N LYS 366
                               74.440 18.365 16.873 1.00 26.99
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ATOM 1609 CA LYS 366
                               75.230 19.577 17.061 1.00 30.69
    ATOM 1610 CB LYS 366
                               76.275 19.708 15.957 1.00 28.53
                               77.481 18.804 16.106 1.00 28.89
    ATOM 1611 CG LYS 366
                               78.430 19.027 14.939 1.00 32.51
    ATOM 1612 CD LYS 366
                               79.743 18.294 15.116 1.00 38.52
    ATOM 1613 CE LYS 366
                               80.632 18.506 13.939 1.00 45.28
    ATOM 1614 NZ LYS 366
                               74.349 20.831 17.079 1.00 36.18
    ATOM 1615 C LYS 366
                               74.472 21.672 17.972 1.00 39.82
    ATOM 1616 O LYS 366
                               73.464 20.950 16.091 1.00 37.54
    ATOM 1617 N LEU 367
                                72.557 22.092 15.994 1.00 36.14
    ATOM 1618 CA LEU 367
10
    ATOM 1619 CB LEU 367
                               71.803 22.070 14.659 1.00 32.20
                                70.764 23.179 14.447 1.00 36.16
    ATOM 1620 CG LEU 367
                                71,402 24,567 14,618 1.00 20,60
    ATOM 1621 CD1 LEU 367
    ATOM 1622 CD2 LEU 367
                                70.139 23.030 13.065 1.00 34.30
                               71.561 22.060 17.143 1.00 36.84
    ATOM 1623 C LEU 367
15
                               71.231 23.091 17.729 1.00 36.94
    ATOM 1624 O LEU 367
                               71.083 20.866 17.459 1.00 37.81
    ATOM 1625 N LEU 368
                               70.130 20.683 18.536 1.00 34.83
    ATOM 1626 CA LEU 368
                               69.763 19.205 18.622 1.00 36.98
    ATOM 1627 CB LEU 368
    ATOM 1628 CG LEU 368
                                68.421 18.777 19.205 1.00 40.34
20
                                67.276 19.595 18.619 1.00 36.28
    ATOM 1629 CD1 LEU 368
                                68.241 17.299 18.908 1.00 39.39
    ATOM 1630 CD2 LEU 368
                               70.755 21.182 19.843 1.00 38.32
    ATOM 1631 C LEU 368
    ATOM 1632 O LEU 368
                               70.059 21.711 20.707 1.00 41.87
                               72.075 21.057 19.962 1.00 39.46
    ATOM 1633 N MET 369
25
                                72.790 21.515 21.154 1.00 40.12
    ATOM 1634 CA MET 369
                                74.219 20.971 21.168 1.00 41.26
    ATOM 1635 CB MET 369
    ATOM 1636 CG MET 369
                                74.307 19.493 21.521 1.00 47.83
                                75.961 18.810 21.289 1.00 55.72
    ATOM 1637 SD MET 369
                                76.809 19.474 22.727 1.00 54.37
    ATOM 1638 CE MET 369
30
                               72.805 23.039 21.251 1.00 42.81
    ATOM 1639 C MET 369
                               72.990 23.601 22.335 1.00 47.81
    ATOM 1640 O MET 369
                               72.622 23.708 20.115 1.00 40.09
    ATOM 1641 N LYS 370
                                72.588 25.165 20.080 1.00 33.65
    ATOM 1642 CA LYS 370
                                72.751 25.677 18.650 1.00 30.83
    ATOM 1643 CB LYS 370
35
                                74.138 25.435 18.078 1.00 30.98
    ATOM 1644 CG LYS 370
                                75.188 26.198 18.867 1.00 37.82
    ATOM 1645 CD LYS 370
     ATOM 1646 CE LYS 370
                                76.591 25.938 18.351 1.00 36.05
                                77.034 24.562 18.667 1.00 48.68
     ATOM 1647 NZ LYS 370
                               71.293 25.684 20.702 1.00 33.32
     ATOM 1648 C LYS 370
40
                               71.218 26.842 21.112 1.00 34.75
     ATOM 1649 O LYS 370
                               70.277 24.826 20.779 1.00 31.90
     ATOM 1650 N VAL 371
                                69.006 25.197 21.395 1.00 31.77
     ATOM 1651 CA VAL 371
                                67.933 24.092 21.214 1.00 30.28
     ATOM 1652 CB. VAL 371
                                66.673 24.429 21.995 1.00 30.02
     ATOM 1653 CG1 VAL 371
45
                                67.596 23.933 19.746 1.00 32.23
     ATOM 1654 CG2 VAL 371
                               69.277 25.417 22.885 1.00 34.44
     ATOM 1655 C VAL 371
                               68.722 26.331 23.499 1.00 33.35
     ATOM 1656 O VAL 371
     ATOM 1657 N THR 372
                               70.161 24.590 23.443 1.00 33.15
                               70.551 24.675 24.847 1.00 32.47
     ATOM 1658 CA THR 372
50
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ATOM 1659 CB THR 372
                                71.541 23.556 25.207 1.00 32.11
                                70.955 22.288 24.891 1.00 35.33
    ATOM 1660 OG1 THR 372
                                71.894 23.603 26.688 1.00 32.54
    ATOM 1661 CG2 THR 372
                               71.226 26.020 25.108 1.00 34.49
    ATOM 1662 C THR 372
                               70.936 26.696 26.099 1.00 34.07
    ATOM 1663 O THR 372
                               72.120 26.405 24.202 1.00 32.77
    ATOM 1664 N ASP 373
                               72.830 27.671 24.315 1.00 28.08
    ATOM 1665 CA ASP 373
                               73,803 27,841 23,147 1,00 31,59
    ATOM 1666 CB ASP 373
                                74.910 26.789 23.142 1.00 37.29
    ATOM 1667 CG ASP 373
                                75.170 26.169 24.196 1.00 40.82
    ATOM 1668 OD1 ASP 373
10
    ATOM 1669 OD2 ASP 373
                                75.531 26.586 22.079 1.00 40.81
                               71.830 28.821 24.353 1.00 29.21
    ATOM 1670 C ASP 373
    ATOM 1671 O ASP 373
                               71.931 29.709 25.200 1.00 31.85
    ATOM 1672 N LEU 374
                               70.843 28.775 23.463 1.00 24.71
                                69.813 29.802 23.403 1.00 25.25
    ATOM 1673 CA LEU 374
15
                                68.906 29.587 22.188 1.00 25.61
    ATOM 1674 CB LEU 374
                                69.480 30.084 20.858 1.00 25.51
    ATOM 1675 CG LEU 374
                                68.741 29.469 19.677 1.00 23.53
    ATOM 1676 CD1 LEU 374
    ATOM 1677 CD2 LEU 374
                                69.405 31.596 20.820 1.00 21.92
    ATOM 1678 C LEU 374
                               68.994 29.827 24.686 1.00 26.84
20
                               68.591 30.895 25.151 1.00 28.96
    ATOM 1679 O LEU 374
                               68.746 28.651 25.254 1.00 31.00
    ATOM 1680 N ARG 375
                                67.996 28.554 26.502 1.00 32.86
    ATOM 1681 CA ARG 375
    ATOM 1682 CB ARG 375
                                67.831 27.090 26.924 1.00 36.80
                                66.861 26.297 26.071 1.00 44.91
    ATOM 1683 CG ARG 375
25
                                65.433 26.731 26.338 1.00 58.99
    ATOM 1684 CD ARG 375
                                64.501 26.210 25.342 1.00 72.26
    ATOM 1685 NE ARG 375
                                63.909 25.020 25.404 1.00 77.46
    ATOM 1686 CZ ARG 375
    ATOM 1687 NH1 ARG 375
                                 64.147 24.201 26.422 1.00 80.94
                                 63.062 24.657 24.447 1.00 75.58
    ATOM 1688 NH2 ARG 375
30
                               68.771 29.317 27.570 1.00 32.27
     ATOM 1689 C ARG 375
                               68.199 30.125 28.304 1.00 33.75
     ATOM 1690 O ARG 375
                                70.084 29.098 27.602 1.00 32.65
     ATOM 1691 N MET 376
                                70.967 29.753 28.560 1.00 35.83
     ATOM 1692 CA MET 376
     ATOM 1693 CB MET 376
                                72.392 29.210 28.434 1.00 39.25
35
                                72.526 27.751 28.839 1.00 54.45
     ATOM 1694 CG MET 376
                                74.245 27.212 28.944 1.00 73.93
     ATOM 1695 SD MET 376
     ATOM 1696 CE MET 376
                                74.421 26.270 27.434 1.00 67.01
                               70.960 31.267 28.378 1.00 35.38
     ATOM 1697 C MET 376
                                70.882 32.015 29.353 1.00 34.73
     ATOM 1698 O MET 376
40
                              71.038 31.716 27.129 1.00 32.51
     ATOM 1699 N ILE 377
     ATOM 1700 CA ILE 377
                               71.016 33.142 26.816 1.00 26.55
                               71.182 33.370 25.299 1.00 24.84
     ATOM 1701 CB ILE 377
     ATOM 1702 CG2 ILE 377
                                70.817 34.797 24.923 1.00 26.63
                                72.616 33.038 24.890 1.00 20.66
     ATOM 1703 CG1 ILE 377
45
     ATOM 1704 CD1 ILE 377
                                72.872 33.104 23.409 1.00 20.74
                              69.706 33.755 27.313 1.00 25.47
     ATOM 1705 C ILE 377
     ATOM 1706 O ILE 377
                              69.696 34.848 27.881 1.00 29.99
     ATOM 1707 N GLY 378
                               68.608 33.033 27.127 1.00 25.11
                                67.321 33.522 27.580 1.00 27.82
     ATOM 1708 CA GLY 378
50
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ATOM 1709 C GLY 378
                               67.279 33.613 29.095 1.00 30.90
                               66.749 34.579 29.651 1.00 31.19
    ATOM 1710 O GLY 378
                               67.851 32.611 29.761 1.00 31.62
     ATOM 1711 N ALA 379
                                67.896 32.547 31.223 1.00 30.74
    ATOM 1712 CA ALA 379
                                68.433 31.198 31.671 1.00 30.82
     ATOM 1713 CB ALA 379
                               68.756 33.668 31.801 1.00 30.07
     ATOM 1714 C ALA 379
                               68.327 34.384 32.708 1.00 31.05
     ATOM 1715 O ALA 379
                               69.966 33.817 31.273 1.00 29.72
     ATOM 1716 N CYA 380
                                70.873 34.866 31.723 1.00 33.36
    ATOM 1717 CA CYA 380
                                72.201 34.809 30.963 1.00 38.31
     ATOM 1718 CB CYA 380
10
                                73.249 33.407 31.386 1.00 50.99
    ATOM 1719 SG CYA 380
                                74.982 33.655 29.929 1.00 70.37
     ATOM 1720 AS CYA 380
                               70.226 36.232 31.535 1.00 33.40
     ATOM 1721 C CYA 380
                               70.246 37.062 32.442 1.00 36.41
     ATOM 1722 O CYA 380
    ATOM 1723 N HIS 381
                              69.615 36.456 30.374 1.00 32.55
                               68.965 37.734 30.114 1.00 26.41
     ATOM 1724 CA HIS 381
                               68.434 37.811 28.681 1.00 20.89
     ATOM 1725 CB HIS 381
     ATOM 1726 CG HIS 381
                               67.593 39.023 28.423 1.00 15.78
     ATOM 1727 CD2 HIS 381
                                67.928 40.277 28.041 1.00 12.67
                                66.226 39.031 28.605 1.00 17.88
     ATOM 1728 ND1 HIS 381
20
                                65.756 40.239 28.353 1.00 16.27
     ATOM 1729 CE1 HIS 381
                                66.768 41.013 28.008 1.00 17.18
     ATOM 1730 NE2 HIS 381
     ATOM 1731 C HIS 381
                              67.839 38.023 31.102 1.00 26.73
     ATOM 1732 O HIS 381
                              67.621 39.176 31.464 1.00 30.46
                               67.111 36.991 31.521 1.00 26.68
     ATOM 1733 N ALA 382
25
                                66.010 37.176 32.464 1.00 27.90
     ATOM 1734 CA ALA 382
                                65.237 35.878 32.642 1.00 25.29
     ATOM 1735 CB ALA 382
                               66.511 37.697 33.810 1.00 31.23
     ATOM 1736 C ALA 382
     ATOM 1737 O ALA 382
                               65.927 38.617 34.378 1.00 37.67
                               67.596 37.114 34.316 1.00 34.15
     ATOM 1738 N SER 383
30
                                68.174 37.550 35.588 1.00 37.23
     ATOM 1739 CA SER 383
                                69.294 36.605 36.027 1.00 40.21
     ATOM 1740 CB SER 383
     ATOM 1741 OG SER 383
                                68.785 35.324 36.361 1.00 53.99
                               68.727 38.958 35.417 1.00 33.67
     ATOM 1742 C SER 383
                               68.532 39.827 36.268 1.00 40.73
     ATOM 1743 O SER 383
35
                                69.411 39.171 34.298 1.00 29.95
     ATOM 1744 N ARG 384
                                70.000 40.458 33.957 1.00 29.77
     ATOM 1745 CA ARG 384
     ATOM 1746 CB ARG 384
                                70.684 40.350 32.594 1.00 30.79
     ATOM 1747 CG ARG 384
                                71.481 41.558 32.167 1.00 31.34
                                72.781 41.638 32.918 1.00 33.62
     ATOM 1748 CD ARG 384
40
                                73.657 42.660 32.358 1.00 41.68
     ATOM 1749 NE ARG 384
                                74.584 43.310 33.052 1.00 41.20
     ATOM 1750 CZ ARG 384
                                 74.756 43.047 34.339 1.00 42.11
     ATOM 1751 NH1 ARG 384
                                 75.349 44.213 32.455 1.00 37.27
     ATOM 1752 NH2 ARG 384
                                68.910 41.536 33.911 1.00 35.72
45
     ATOM 1753 C ARG 384
     ATOM 1754 O ARG 384
                                69.090 42.635 34.439 1.00 41.66
                               67.768 41.196 33.318 1.00 34.30
     ATOM 1755 N PHE 385
                                66.646 42.119 33.199 1.00 32.40
     ATOM 1756 CA PHE 385
     ATOM 1757 CB PHE 385
                                65.527 41.502 32.356 1.00 29.02
                                64.344 42.407 32.163 1.00 26.56
50 · ATOM 1758 CG PHE 385
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ATOM 1759 CD1 PHE 385
                                64.317 43.320 31.119 1.00 26.59
                                63.263 42.355 33.037 1.00 24.69
    ATOM 1760 CD2 PHE 385
                                63.231 44.173 30.947 1.00 31.70
    ATOM 1761 CE1 PHE 385
    ATOM 1762 CE2 PHE 385
                                62.174 43.202 32.875 1.00 26.79
    ATOM 1763 CZ PHE 385
                               62.158 44.115 31.827 1.00 31.59
                               66.121 42.492 34.578 1.00 32.98
    ATOM 1764 C PHE 385
    ATOM 1765 O PHE 385
                               65.822 43.659 34.839 1.00 33.91
                               66.003 41.499 35.456 1.00 33.91
    ATOM 1766 N LEU 386
                               65.533 41.736 36.818 1.00 38.66
    ATOM 1767 CA LEU 386
                               65.547 40.440 37.633 1.00 43.79
    ATOM 1768 CB LEU 386
10
                                64.327 39.521 37.525 1.00 49.81
    ATOM 1769 CG LEU 386
                                64.652 38.147 38.099 1.00 51.12
    ATOM 1770 CD1 LEU 386
                                63.135 40.148 38.246 1.00 49.17
    ATOM 1771 CD2 LEU 386
    ATOM 1772 C LEU 386
                               66,445 42.761 37.475 1.00 38.95
    ATOM 1773 O LEU 386
                               65,979 43.682 38.146 1.00 42.16
15
                              67.745 42.613 37.248 1.00 33.62
    ATOM 1774 N HIS 387
                               68.723 43.531 37.808 1.00 39.73
    ATOM 1775 CA HIS 387
                               70.138 42.980 37.639 1.00 40.71
    ATOM 1776 CB HIS 387
    ATOM 1777 CG HIS 387
                               70.403 41.749 38.449 1.00 52.03
                               69.573 40.967 39.181 1.00 53.85
    ATOM 1778 CD2 HIS 387
20
                                71.657 41.189 38.566 1.00 54.79
    ATOM 1779 ND1 HIS 387
    ATOM 1780 CE1 HIS 387
                               71.590 40.114 39.334 1.00 56.55
     ATOM 1781 NE2 HIS 387
                                70.336 39.958 39.720 1.00 57.48
     ATOM 1782 C HIS 387
                              68.594 44.913 37.175 1.00 42.08
                               68.712 45.926 37.865 1.00 44.12
    ATOM 1783 O HIS 387
25
                               68.318 44.957 35.874 1.00 42.38
    ATOM 1784 N MET 388
                                68.154 46.229 35.175 1.00 38.00
    ATOM 1785 CA MET 388
     ATOM 1786 CB MET 388
                                67.840 46.006 33.692 1.00 40.21
                                69.009 45.555 32.829 1.00 41.26
     ATOM 1787 CG MET 388
                                68.500 45.427 31.089 1.00 45.51
    ATOM 1788 SD MET 388
30
                                69.089 43.802 30.645 1.00 42.40
     ATOM 1789 CE MET 388
                               67.025 47.044 35.810 1.00 38.11
     ATOM 1790 C MET 388
                               67.155 48.255 35.997 1.00 38.41
     ATOM 1791 O MET 388
                               65.926 46.374 36.144 1.00 39.67
     ATOM 1792 N LYS 389
                                64.773 47.036 36.750 1.00 44.96
    ATOM 1793 CA LYS 389
35
                                63,570 46.087 36.818 1.00 49.52
     ATOM 1794 CB LYS 389
                                62.674 46.102 35.588 1.00 56.74
     ATOM 1795 CG LYS 389
                                62.145 47.509 35.278 1.00 68.05
     ATOM 1796 CD LYS 389
                                61.287 48.100 36.403 1.00 71.47
     ATOM 1797 CE LYS 389
                                60.038 47.330 36.661 1.00 71.98
     ATOM 1798 NZ LYS 389
40
                               65.041 47.604 38.141 1.00 46.60
     ATOM 1799 C LYS 389
                               64.516 48.661 38.499 1.00 47.25
     ATOM 1800 O LYS 389
                               65.832 46.893 38.935 1.00 47.15
     ATOM 1801 N VAL 390
                                66.129 47.353 40.284 1.00 50.75
     ATOM 1802 CA VAL 390
                                66.686 46.202 41.182 1.00 50.42
     ATOM 1803 CB VAL 390
45
                                68.095 45.802 40.770 1.00 47.93
     ATOM 1804 CG1 VAL 390
     ATOM 1805 CG2 VAL 390
                                 66.650 46.612 42.640 1.00 56.67
                               67.072 48.558 40.286 1.00 49.82
     ATOM 1806 C VAL 390
                               66,971 49,426 41.152 1.00 52.44
     ATOM 1807 O VAL 390
                               67.926 48.651 39.272 1.00 46.14
     ATOM 1808 N GLU 391
50
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	ATOM	1809 CA GLU 391	68.888 49.741 39.173 1.00 43.84
	ATOM	1810 CB GLU 391	70.150 49.268 38.449 1.00 41.44
	ATOM	1811 CG GLU 391	70.837 48.074 39.095 1.00 51.12
	ATOM	1812 CD GLU 391	71.218 48.325 40.540 1.00 57.29
5	ATOM	1813 OE1 GLU 391	71.970 49.287 40.802 1.00 58.15
	ATOM	1814 OE2 GLU 391	70.764 47.559 41.416 1.00 62.51
	ATOM	1815 C GLU 391	68.386 51.015 38.501 1.00 45.94
	ATOM	1816 O GLU 391	68.567 52.114 39.033 1.00 51.14
	ATOM	1817 N CYA 392	67.727 50.872 37.354 1.00 45.84
10	ATOM	1818 CA CYA 392	67.255 52.029 36.598 1.00 41.60
	ATOM	1819 CB CYA 392	67.681 51.889 35.140 1.00 42.06
	ATOM	1820 SG CYA 392	69.452 52.008 34.968 1.00 44.47
	ATOM	1821 AS CYA 392	69.867 50.812 33.150 1.00 54.22
	ATOM	1822 C CYA 392	65.779 52.395 36.683 1.00 42.27
15	ATOM	1823 O CYA 392	64.937 51.564 37.029 1.00 43.91
	ATOM	1824 N PRO 393	65.451 53.674 36.414 1.00 42.79
	ATOM	1825 CD PRO 393	66.384 54.774 36.106 1.00 38.59
	ATOM	1826 CA PRO 393	64.067 54.159 36.459 1.00 44.20
	ATOM	1827 CB PRO 393	64.218 55.667 36.238 1.00 39.88
20	ATOM	1828 CG PRO 393	65.487 55.789 35.459 1.00 35.88
	ATOM	1829 C PRO 393	63.178 53.513 35.398 1.00 45.29
	ATOM	1830 O PRO 393	63.600 53.308 34.257 1.00 43.97
	ATOM	1831 N THR 394	61.935 53.238 35.782 1.00 48.20
	ATOM	1832 CA THR 394	60.959 52.607 34.901 1.00 53.71
25	ATOM	1833 CB THR 394	59.605 52.429 35.629 1.00 59.59
	ATOM	1834 OG1 THR 394	58.690 51.717 34.787 1.00 66.50
	ATOM	1835 CG2 THR 394	59.013 53.787 36.004 1.00 61.00
	ATOM	1836 C THR 394	60.752 53.358 33.581 1.00 51.35
	ATOM	1837 O THR 394	60.419 52.751 32.563 1.00 54.39
30	ATOM	1838 N GLU 395	61.008 54.664 33.595 1.00 47.65
	ATOM	1839 CA GLU 395	60.845 55.509 32.414 1.00 44.43
	ATOM	1840 CB GLU 395	60.988 56.978 32.804 1.00 43.85 61.788 55.175 31.250 1.00 42.93
	ATOM	1841 C GLU 395	61.589 55.649 30.129 1.00 42.93
25	ATOM	1842 O GLU 395	62.818 54.375 31.517 1.00 39.38
35	ATOM	1843 N LEU 396	63.782 53.989 30.486 1.00 35.70
	ATOM ATOM	1844 CA LEU 396 1845 CB LEU 396	65.185 53.867 31.090 1.00 34.96
			65.854 55.141 31.609 1.00 36.47
	ATOM	1846 CG LEU 396 1847 CD1 LEU 396	67.234 54.807 32.150 1.00 34.21
40	ATOM	1848 CD2 LEU 396	65.959 56.164 30.491 1.00 32.74
40	ATOM	1849 C LEU 396	63.407 52.671 29.803 1.00 34.60
	ATOM ATOM	1850 O LEU 396	64.086 52.223 28.873 1.00 30.36
	ATOM	1851 N PHE 397	62.325 52.059 30.269 1.00 33.02
	ATOM	1852 CA PHE 397	61.868 50.792 29.725 1.00 33.39
15	ATOM	1853 CB PHE 397	61.615 49.782 30.852 1.00 34.30
45	ATOM	1854 CG PHE 397	62.834 49.439 31.665 1.00 32.62
	ATOM	1855 CD1 PHE 397	63.296 50.301 32.654 1.00 32.35
	ATOM	1856 CD2 PHE 397	63.504 48.241 31.461 1.00 31.28
	ATOM	1857 CEI PHE 397	64.407 49.976 33.426 1.00 27.01
50	ATOM	1858 CE2 PHE 397	64.616 47.905 32.229 1.00 33.34
JU	AIOM	1030 CE2 FILE 397	UT.UIU T7.705 52.227 1.00 55.5T

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ATOM 1859 CZ PHE 397
                               65.067 48.775 33.213 1.00 31.29
                              60.580 50.961 28.934 1.00 33.17
    ATOM 1860 C PHE 397
                               59.540 51.318 29.498 1.00 31.99
    ATOM 1861 O PHE 397
                               60.636 50.752 27.606 1.00 32.45
    ATOM 1862 N PRO 398
                               61.821 50.493 26.768 1.00 28.15
    ATOM 1863 CD PRO 398
                               59.429 50.885 26.786 1.00 30.02
    ATOM 1864 CA PRO 398
                               59.921 50.483 25.394 1.00 28.15
    ATOM 1865 CB PRO 398
    ATOM 1866 CG PRO 398
                               61.352 50.923 25.397 1.00 24.89
                               58.384 49.900 27.326 1.00 28.39
    ATOM 1867 C PRO 398
                               58.735 48.810 27.789 1.00 28.00
    ATOM 1868 O PRO 398
10
                               57.092 50.262 27.267 1.00 32.45
    ATOM 1869 N PRO 399
                               56.577 51.511 26.672 1.00 34.93
    ATOM 1870 CD PRO 399
                               55.989 49.421 27.753 1.00 32.54
    ATOM 1871 CA PRO 399
                               54,755 50.122 27.188 1.00 34.47
    ATOM 1872 CB PRO 399
    ATOM 1873 CG PRO 399
                               55.159 51.564 27.196 1.00 31.37
                               56.044 47.946 27.338 1.00 32.18
    ATOM 1874 C PRO 399
    ATOM 1875 O PRO 399
                               55.950 47.054 28.188 1.00 32.58
                               56.195 47.689 26.041 1.00 30.15
    ATOM 1876 N LEU 400
    ATOM 1877 CA LEU 400
                               56.259 46.314 25.541 1.00 32.32
    ATOM 1878 CB LEU 400
                               56.211 46.297 24.011 1.00 28.67
20
                               56.028 44.927 23.351 1.00 28.77
    ATOM 1879 CG LEU 400
                                54.802 44.234 23.919 1.00 22.73
    ATOM 1880 CD1 LEU 400
                                55.897 45.096 21.846 1.00 27.89
    ATOM 1881 CD2 LEU 400
    ATOM 1882 C LEU 400
                               57.496 45.561 26.051 1.00 32.27
    ATOM 1883 O LEU 400
                               57.437 44.358 26.307 1.00 32.87
25
                               58.602 46.279 26.215 1.00 32.27
    ATOM 1884 N PHE 401
                               59.847 45.695 26.710 1.00 32.39
    ATOM 1885 CA PHE 401
                               60.946 46.769 26.711 1.00 31.38
    ATOM 1886 CB PHE 401
    ATOM 1887 CG PHE 401
                               62.290 46.286 27.194 1.00 35.12
                                62.835 45.089 26.729 1.00 34.68
    ATOM 1888 CD1 PHE 401
30
                                63.030 47.051 28.097 1.00 34.57
    ATOM 1889 CD2 PHE 401
                                64.100 44.662 27.155 1.00 30.27
    ATOM 1890 CE1 PHE 401
    ATOM 1891 CE2 PHE 401
                                64.291 46.635 28.526 1.00 33.57
    ATOM 1892 CZ PHE 401
                               64.828 45.438 28.054 1.00 35.74
                               59.599 45.169 28.129 1.00 32.21
    ATOM 1893 C PHE 401
35
                               60.002 44.056 28.478 1.00 33.36
    ATOM 1894 O PHE 401
                               58.902 45.967 28.929 1.00 31.85
    ATOM 1895 N LEU 402
                               58.582 45.602 30.302 1.00 35.06
    ATOM 1896 CA LEU 402
    ATOM 1897 CB LEU 402
                               57.948 46.789 31.029 1.00 34.76
                                58.878 47.852 31.591 1.00 33.48
    ATOM 1898 CG LEU 402
                                58.060 49.010 32.152 1.00 32.58
    ATOM 1899 CD1 LEU 402
                                59.753 47.217 32.662 1.00 26.27
    ATOM 1900 CD2 LEU 402
                               57.626 44.426 30.393 1.00 36.80
    ATOM 1901 C LEU 402
                               57.793 43.545 31.239 1.00 35.43
    ATOM 1902 O LEU 402
                               56.600 44.443 29.547 1.00 38.50
    ATOM 1903 N GLU 403
45
    ATOM 1904 CA GLU 403
                               55.581 43.401 29.540 1.00 40.24
                                54.435 43.792 28.605 1.00 44.03
     ATOM 1905 CB GLU 403
                                53.239 42.850 28.666 1.00 55.53
     ATOM 1906 CG GLU 403
                                52.180 43.159 27.618 1.00 66.67
     ATOM 1907 CD GLU 403
                                52.151 44.299 27.095 1.00 70.81
    ATOM 1908 OE1 GLU 403
50
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	ATOM ATOM	1909 OE2 GLU 403 1910 C GLU 403	51.370 42.255 27.315 1.00 73.80 56.096 42.018 29.162 1.00 38.00
	ATOM	1911 O GLU 403	55.745 41.029 29.805 1.00 38.78
	ATOM	1912 N VAL 404	56.934 41.955 28.132 1.00 37.39
5	ATOM	1913 CA VAL 404	57.475 40.686 27.652 1.00 37.05
	ATOM	1914 CB VAL 404	58.180 40.855 26.286 1.00 35.57
	ATOM	1915 CG1 VAL 404	58.677 39.513 25.776 1.00 36.85
	ATOM	1916 CG2 VAL 404	57.222 41.451 25.287 1.00 42.03
	ATOM	1917 C VAL 404	58.438 40.000 28.609 1.00 38.69
10	ATOM	1918 O VAL 404	58.436 38.774 28.727 1.00 40.71
	ATOM	1919 N PHE 405	59.267 40.785 29.286 1.00 39.34
	ATOM	1920 CA PHE 405	60.250 40.221 30.198 1.00 39.33
	ATOM	1921 CB PHE 405	61.620 40.840 29.913 1.00 33.87
	ATOM	1922 CG PHE 405	62.107 40.609 28.509 1.00 32.17
15	ATOM	1923 CD1 PHE 405	62.355 41.683 27.660 1.00 31.34
	ATOM	1924 CD2 PHE 405	62.315 39.317 28.032 1.00 31.98
	ATOM	1925 CE1 PHE 405	62.801 41.476 26.352 1.00 30.79
	ATOM	1926 CE2 PHE 405	62.759 39.099 26.730 1.00 26.06
	ATOM	1927 CZ PHE 405	63.004 40.182 25.889 1.00 27.98
20	ATOM	1928 C PHE 405	59.905 40.322 31.682 1.00 42.64
	ATOM	1929 O PHE 405	60.785 40.188 32.534 1.00 45.10
	ATOM	1930 N GLU 406	58.630 40.536 31.988 1.00 48.95 58.181 40.641 33.373 1.00 56.93
	ATOM	1931 CA GLU 406	56.820 41.324 33.432 1.00 56.94
25	ATOM	1932 CB GLU 406	58.116 39.263 34.040 1.00 61.92
25	ATOM	1933 C GLU 406	57.988 38.256 33.308 1.00 67.61
	ATOM	1934 O GLU 406 1 O1 HOH 501	67.588 36.828 11.225 1.00 27.32
	ATOM ATOM	2 O1 HOH 502	68.647 41.203 12.940 1.00 39.54
	ATOM	3 O1 HOH 503	64.072 40.115 12.407 1.00 32.47
30	ATOM	4 O1 HOH 504	62.312 39.659 16.075 1.00 17.39
30	ATOM	5 O1 HOH 505	63.449 46.468 15.530 1.00 30.46
	ATOM	6 O1 HOH 506	67.191 15.561 -0.279 1.00 35.96
	ATOM	7 O1 HOH 507	67.100 11.855 0.295 1.00 20.00
	ATOM	8 O1 HOH 508	61.004 15.510 0.047 1.00 20.00
35	ATOM	9 O1 HOH 509	59.851 10.761 6.050 1.00 20.00
	ATOM	10 O1 HOH 510	57.553 11.824 10.360 1.00 44.63
	ATOM	11 O1 HOH 511	54.101 13.545 8.720 1.00 20.00
	ATOM	12 O1 HOH 512	55.923 15.916 12.205 1.00 29.31
	ATOM	13 O1 HOH 513	50.900 19.934 8.193 1.00 20.00
40	ATOM	14 O1 HOH 514	50.474 22.912 7.942 1.00 45.34
	ATOM	15 O1 HOH 515	49.737 20.631 11.530 1.00 20.00
	ATOM	16 O1 HOH 516	50.829 25.467 13.330 1.00 20.00
	ATOM	17 O1 HOH 517	53.818 25.833 10.682 1.00 42.12
	ATOM	18 O1 HOH 518	52.591 31.216 7.313 1.00 35.55
45	ATOM	19 O1 HOH 519	58.510 31.667 2.158 1.00 20.00
	ATOM	20 O1 HOH 520	58.235 36.751 2.232 1.00 20.00
	ATOM	21 O1 HOH 521	62.484 37.992 5.537 1.00 20.00
	ATOM	22 O1 HOH 522	68.184 36.969 5.889 1.00 50.08
	ATOM	23 O1 HOH 523	66.889 33.781 8.584 1.00 20.00
50	ATOM	24 O1 HOH 524	67.217 30.836 3.085 1.00 34.44

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64.336 28.325 3.098 1.00 20.00
             25 O1 HOH 525
    ATOM
             26 O1 HOH 526
                               67.667 26.625 1.519 1.00 20.00
    ATOM
                               76.757 22.883 5.467 1.00 36.94
             27 O1 HOH 527
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                               72.250 17.936 6.950 1.00 36.00
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    ATOM
                               71.760 14.791 8.058 1.00 40.18
             29 O1 HOH 529
    ATOM
             30 O1 HOH 530
                               72.884 14.751 11.484 1.00 41.44
    ATOM
                               69.235 12.986 11.709 1.00 39.38
             31 O1 HOH 531
    ATOM
                               69.402 12.036 14.891 1.00 40.68
             32 O1 HOH 532
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                               64.560 10.910 15.076 1.00 20.00
             33 O1 HOH 533
    ATOM
                               63.169 10.413 11.722 1.00 20.00
             34 O1 HOH 534
    ATOM
10
                               66.042 11.455 11.077 1.00 41.05
             35 O1 HOH 535
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             36 O1 HOH 536
                               81.094 22.520 13.435 1.00 48.70
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    ATOM
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             38 O1 HOH 538
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                               76.420 30.760 23.658 1.00 29.63
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             41 O1 HOH 541
             42 O1 HOH 542
                               83.028 32.743 20.922 1.00 38.14
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     ATOM
                               77.484 34.040 9.664 1.00 36.37
             44 O1 HOH 544
20
    ATOM
                               75.904 32.986 12.256 1.00 34.93
    ATOM
             45 O1 HOH 545
     ATOM
             46 O1 HOH 546
                               74.185 29.689 9.761 1.00 38.60
             47 O1 HOH 547
                               64.936 20.644 23.365 1.00 36.83
     ATOM
                               61.750 22.313 25.288 1.00 34.81
             48 O1 HOH 548
     ATOM
                               59.544 21.463 26.162 1.00 20.00
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                               62.300 27.528 24.386 1.00 35.89
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                               58.228 29.424 24.603 1.00 25.47
             51 O1 HOH 551
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                               57.368 32.196 30.527 1.00 45.27
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             53 O1 HOH 553
                               64.722 36.725 28.906 1.00 24.66
             54 O1 HOH 554
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30
                               62.207 35.851 26.642 1.00 30.36
             55 O1 HOH 555
     ATOM
                               63.608 33.715 25.707 1.00 42.74
             56 O1 HOH 556
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             57 O1 HOH 557
                               62.979 38.422 32.977 1.00 49.93
     ATOM
                               66.911 33.364 34.901 1.00 50.02
             58 O1 HOH 558
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                               72.608 29.636 31.674 1.00 37.60
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             59 O1 HOH 559
35
                               76.967 40.633 32.514 1.00 44.81
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             60 O1 HOH 560
                               73.613 41.817 36.847 1.00 31.79
             61 O1 HOH 561
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                               75.773 46.227 30.514 1.00 29.06
             62 O1 HOH 562
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             63 O1 HOH 563
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             64 O1 HOH 564
                               69.746 51.175 33.564 1.00 20.00
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40
                               74.320 52.047 39.438 1.00 20.00
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                               65.900 53.647 27.404 1.00 40.45
     ATOM
             66 O1 HOH 566
                               68.848 53.076 17.895 1.00 39.25
             67 O1 HOH 567
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                               64.625 46.825 10.331 1.00 20.00
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             69 O1 HOH 569
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                               56.990 49.485 24.052 1.00 37.30
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             72 O1 HOH 572
                               54.188 47.024 30.900 1.00 52.93
             73 O1 HOH 573
     ATOM
                               57.823 44.590 34.025 1.00 53.64
             74 O1 HOH 574
     ATOM
50
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	ATOM	75 O1 HOH 575	47.827 29.597 30.690 1.00 37.61
	ATOM	76 O1 HOH 576	53.030 24.901 32.732 1.00 45.06
	ATOM	77 O1 HOH 577	47.569 19.105 28.647 1.00 38.88
	ATOM	78 O1 HOH 578	47.232 20.282 25.561 1.00 20.00
5	ATOM	79 O1 HOH 579	51.960 14.869 25.534 1.00 49.45
	ATOM	80 O1 HOH 580	52.831 23.395 1.634 1.00 20.00
	ATOM	81 O1 HOH 581	51.472 22.968 -0.900 1.00 25.10
	ATOM	82 O1 HOH 582	77.238 52.503 8.906 1.00 47.05
	END	•	
10	ATOM	2004 C1 DMT 1	67.320 42.326 18.648 1.00 28.58
	ATOM	2005 C2 DMT 1	68.927 43.263 23.318 1.00 29.26
	ATOM	2006 C3 DMT 1	67.236 43.583 19.236 1.00 24.54
	ATOM	2007 C4 DMT 1	69.268 44.313 24.111 1.00 28.48
	ATOM	2008 C5 DMT 1	68.003 43.859 20.363 1.00 28.76
15	ATOM	2009 C6 DMT 1	68.654 44.389 25.458 1.00 28.16
	ATOM	2010 C7 DMT 1	68.811 42.902 20.875 1.00 26.80
	ATOM	2011 C8 DMT 1	67.803 43.410 25.793 1.00 29.83
	ATOM	2012 C9 DMT 1	68.921 41.665 20.324 1.00 26.77
	ATOM	2013 C10 DMT 1	67.464 42.358 24.989 1.00 28.60
20	ATOM	2014 C11 DMT 1	68.165 41.349 19.185 1.00 25.29
	ATOM	2015 C12 DMT 1	68.059 42.281 23.675 1.00 26.74
	ATOM	2016 C13 DMT 1	66.475 42.038 17.456 1.00 21.51
	ATOM	2017 C14 DMT 1	68.916 45.478 26.380 1.00 21.05
	ATOM	2018 C15 DMT 1	66.989 40.910 16.417 1.00 22.84
25	ATOM	2019 C16 DMT 1	68.090 46.870 26.009 1.00 19.41
	ATOM	2020 C17 DMT 1	65.982 40.730 15.243 1.00 27.07
	ATOM	2021 C18 DMT 1	70.279 46.131 26.085 1.00 16.03
	ATOM	2022 C19 DMT 1	67.903 45.249 20.974 1.00 19.56
	ATOM	2023 C20 DMT 1	69.853 40.599 20.901 1.00 4.52
30	ATOM	2024 N1 DMT 1	68.280 41.070 16.042 1.00 17.57
	ATOM	2025 O1 DMT 1	67.209 43.465 27.087 1.00 25.94
	ATOM	2026 O2 DMT 1	69.547 43.191 22.015 1.00 30.23
	ATOM	2027 O3 DMT 1	66.449 40.778 14.118 1.00 29.45
	ATOM	2028 O4 DMT 1	64.820 40.564 15.546 1.00 26.46
35	END		

APPENDIX 4

TR TRIAC.PDB

REMARK

REMARK TR_triac full length numbering

5 REMARK Rfactor 0.236 Rfree 0.241

REMARK Resolution 25. 2.5 all reflections

REMARK

REMARK Three cacodylate-modified cysteines:

REMARK Cys334, Cys380, Cys392

10 REMARK modeled as free arsenic atoms

REMARK

REMARK conserved polar HOH numbered as in TR_t3.pdb

REMARK rearrangements start 600

REMARK

15 REMARK side chain of certain residues modeled as ALA due to poor density;

REMARK however, residue name reflects true residue for clarity

REMARK

REMARK clone obtained from Murray et. al.

REMARK deposited sequence confirmed,

20 REMARK differing from that reported by Thompson et. al.

REMARK in the following codons:

REMARK 281 Thr - Ala

REMARK 285 Lys - Glu

REMARK identical to that reported by Mitsuhashi et. al.

25 REMARK gb:RNTRAVI X07409

JRNL AUTH M.B. MURRAY, N.D.ZILZ,

N.L.MCCREARY, M.J.MACDONALD

JRNL AUTH 2 H.C.TOWLE

JRNL TITL ISOLATION AND CHARACTERIZATION OF RAT CDNA

30 CLONES FOR TWO

JRNL TITL 2 DISTINCT THYROID HORMONE RECPTORS

JRNL REF JBC

V. 263 25 1988

JRNL AUTH C.C.THOMPSON, C.WEINBERGER, R.LEBO, R.M.EVANS

JRNL TITL IDENTIFICATION OF A NOVEL THYROID HORMONE

35 RECEPTOR EXPRESSED

JRNL TITL 2 IN THE MAMMALIAN CENTRAL NERVOUS SYSTEM

JRNL REF SCIENCE

V. 237 1987

JRNL AUTH T.MITSUHASHI,G.TENNYSON,V.NIKODEM

JRNL TITL NUCLEOTIDE SEQUENCE OF NOVEL CDNAS GENERATED

40 BY ALTERNATIVE

JRNL TITL 2 SPLICING OF A RAT THYROID HORMONE RECEPTOR GENE TRANSCRIPT

JRNL REF NUC. ACIDS. RES. V. 16 12 1988 REMARK

45 ATOM 1 CB ARG 157 9.880 -24.199 7.196 1.00 57.79

ATOM 2 CG ARG 157 11.380 -24.411 7.340 1.00 57.79

ATOM 3 CD ARG 157 11.960 -23.602 8.486 1.00 57.79 ATOM 4 NE ARG 157 11.492 -24.098 9.778 1.00 57.79

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	ATOM	5 CZ ARG 157	12.284 -24.379 10.809 1.00 57.79
	ATOM	6 NH1 ARG 157	13.598 -24.212 10.714 1.00 57.79
	ATOM	7 NH2 ARG 157	11.762 -24.854 11.932 1.00 57.79
	ATOM	8 C ARG 157	7.774 -24.838 5.974 1.00 38.50
5	ATOM	9 O ARG 157	7.553 -24.416 4.840 1.00 57.79
	ATOM	10 N ARG 157	9.929 -25.500 5.089 1.00 38.50
	ATOM	11 CA ARG 157	9.183 -25.276 6.360 1.00 38.50
	ATOM	12 N PRO 158	6.802 -24.951 6.895 1.00 23.08
	ATOM	13 CD PRO 158	6.945 -25.424 8.282 1.00 28.38
10	ATOM	14 CA PRO 158	5.415 -24.562 6.617 1.00 23.08
	ATOM	15 CB PRO 158	4.704 -24.824 7.948 1.00 28.38
	ATOM	16 CG PRO 158	5.801 -24.735 8.966 1.00 28.38
	ATOM	17 C PRO 158	5.210 -23.124 6.132 1.00 23.08
	ATOM	18 O PRO 158	5.678 -22.167 6.753 1.00 28.38
15	ATOM	19 N GLU 159	4.504 -23.000 5.012 1.00 19.26
	ATOM	20 CA GLU 159	4.191 -21.717 4.389 1.00 19.26
	ATOM	21 CB GLU 159	4.022 -21.912 2.878 1.00 24.58
•	ATOM	22 CG GLU 159	5.317 -22.009 2.086 1.00 24.58
	ATOM	23 CD GLU 159	5.849 -20.651 1.659 1.00 24.58
20	ATOM	24 OE1 GLU 159	5.034 -19.722 1.476 1.00 24.58
	ATOM	25 OE2 GLU 159	7.080 -20.513 1.490 1.00 24.58
	ATOM	26 C GLU 159	2.879 -21.193 4.968 1.00 19.26
	ATOM	27 O GLU 159	2.152 -21.931 5.636 1.00 24.58
	ATOM	28 N PRO 160	2.579 -19.899 4.765 1.00 17.44 3.442 -18.817 4.259 1.00 13.94
25	ATOM	29 CD PRO 160	1.323 -19.360 5.299 1.00 17.44
	ATOM	30 CA PRO 160	1.414 -17.872 4.956 1.00 13.94
	ATOM	31 CB PRO 160 32 CG PRO 160	2.880 -17.604 4.952 1.00 13.94
	ATOM	32 CG PRO 160 33 C PRO 160	0.098 -20.006 4.639 1.00 17.44
20	ATOM	34 O PRO 160	0.067 -20.207 3.423 1.00 13.94
30	ATOM ATOM	35 N THR 161	-0.895 -20.352 5.450 1.00 17.00
	ATOM	36 CA THR 161	-2.119 -20.957 4.941 1.00 17.00
	ATOM	37 CB THR 161	-2.958 -21.587 6.086 1.00 20.43
	ATOM	38 OG1 THR 161	-3.441 -20.557 6.959 1.00 20.43
35	ATOM	39 CG2 THR 161	-2.121 -22.576 6.888 1.00 20.43
33	ATOM	40 C THR 161	-2.929 -19.843 4.284 1.00 17.00
	ATOM	41 O THR 161	-2.691 -18.660 4.547 1.00 20.43
	ATOM	42 N PRO 162	-3.918 -20.200 3.449 1.00 12.94
	ATOM	43 CD PRO 162	-4.311 -21.559 3.038 1.00 17.56
40	ATOM	44 CA PRO 162	-4.743 -19.190 2.780 1.00 12.94
10	ATOM	45 CB PRO 162	-5.846 -20.029 2.143 1.00 17.56
	ATOM	46 CG PRO 162	-5.147 -21.303 1.816 1.00 17.56
	ATOM	47 C PRO 162	-5.317 -18.171 3.763 1.00 12.94
	ATOM	48 O PRO 162	-5.305 -16.964 3.503 1.00 17.56
45	ATOM	49 N GLU 163	-5.790 -18.668 4.903 1.00 19.45
	ATOM	50 CA GLU 163	-6.374 -17.828 5.943 1.00 19.45
	ATOM	51 CB GLU 163	-6.994 -18.690 7.047 1.00 49.96
	ATOM	52 CG GLU 163	-8.178 -19.558 6.606 1.00 49.96
	ATOM	53 CD GLU 163	-7.782 -20.720 5.697 1.00 49.96
50	ATOM	54 OE1 GLU 163	-6.735 -21.361 5.951 1.00 49.96

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-8.527 -20.999 4.731 1.00 49.96
             55 OE2 GLU 163
     ATOM
     ATOM
             56 C GLU 163
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                               -5.614 -15.731 6.832 1.00 49.96
             57 O GLU 163
     ATOM
                               -4.120 -17.417 6.734 1.00 22.03
     ATOM
             58 N GLU 164
                                -3.033 -16.634 7.305 1.00 22.03
    ATOM
             59 CA GLU 164
             60 CB GLU 164
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             61 CG GLU 164
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             62 CD GLU 164
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    . ATOM
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             65 C GLU 164
     ATOM
                               -2.160 -14.470 6.802 1.00 17.15
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             66 O GLU 164
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             69 CB TRP 165
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             70 CG TRP 165
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     ATOM
             71 CD2 TRP 165
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             75 NE1 TRP 165
     ATOM
             76 CZ2 TRP 165
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             77 CZ3 TRP 165
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                                 3.046 -14.754 1.729 1.00 2.00
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             79 C TRP 165
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     ATOM
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             82 CA ASP 166
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             83 CB ASP 166
     ATOM
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             84 CG ASP 166
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             86 OD2 ASP 166
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     ATOM
             87 C ASP 166
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             88 O ASP 166
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     ATOM
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     ATOM
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             92 CG LEU 167
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             93 CD1 LEU 167
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     ATOM
             94 CD2 LEU 167
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                               -3.120 -10.006 8.367 1.00 31.53
             96 O LEU 167
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                               -2.180 -11.714 7.228 1.00 13.18
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             97 N ILE 168
                               -0.937 -11.027 6.900 1.00 13.18
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             98 CA ILE 168
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                                 1.118 -11.182 5.414 1.00 18.30
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             100 CG2 ILE 168
     ATOM
             101 CG1 ILE 168
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             102 CD1 ILE 168
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             103 C ILE 168
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     ATOM
             104 O ILE 168
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                               -2.342 -8.674 4.245 1.00 12.99
            106 CA HIS 169
    ATOM
                               -3.218 -9.087 3.062 1.00 13.09
            107 CB HIS 169
    ATOM
                               -2.553 -10.045 2.126 1.00 13.09
            108 CG HIS 169
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                               -1.247 -10.223 1.811 1.00 13.09
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                               -3.249 -11.000 1.416 1.00 13.09
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                               -2.403 -11.728 0.710 1.00 13.09
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                               -1.181 -11.277 0.936 1.00 13.09
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                              -2.680 -6.377 4.839 1.00 13.09
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           114 O HIS 169
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                                -5.863 -7.572 7.443 1.00 20.12
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            118 CG1 VAL 170
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                                -6.869 -8.165 6.471 1.00 20.12
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            119 CG2 VAL 170
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     ATOM 122 N ALA 171
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            125 C ALA 171
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                                1.062 -6.032 5.445 1.00 14.17
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                               0.045 -3.936 6.337 1.00 12.51
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                               0.701 -2.910 6.537 1.00 14.17
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            133 O THR 172
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                                -3.823 -1.679 4.171 1.00 49.44
            137 CG GLU 173
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                                -2.930 -0.835 3.266 1.00 49.44
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            139 OE1 GLU 173
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            140 OE2 GLU 173
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                               -1.854 -0.568 6.557 1.00 49.44
            142 O GLU 173
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            143 N ALA 174
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                                -2.798 -1.631 8.957 1.00 13.12
             144 CA ALA 174
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                                -3.226 -2.576 10.068 1.00 17.51
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             145 CB ALA 174
                               -1.556 -0.856 9.375 1.00 13.12
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             146 C ALA 174
            147 O ALA 174
                               -1.634 0.319 9.735 1.00 17.51
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                               -0.409 -1.521 9.317 1.00 12.20
             148 N HIS 175
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                                0.851 -0.895 9.679 1.00 12.20
             149 CA HIS 175
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                                1.944 -1.949 9.886 1.00 17.52
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             150 CB HIS 175
                                3.302 -1.365 10.136 1.00 17.52
             151 CG HIS 175
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                                3.733 -0.468 11.055 1.00 17.52
             152 CD2 HIS 175
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                                4.400 -1.679 9.364 1.00 17.52
             153 ND1 HIS 175
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                                5.447 -0.999 9.793 1.00 17.52
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             154 CE1 HIS 175
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5.070 -0.258 10.818 1.00 17.52
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                               1.735 0.677 6.328 1.00 12.54
            159 CA ARG 176
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            160 CB ARG 176
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                               2.666 -1.565 3.299 1.00 50.41
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            162 CD ARG 176
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            163 NE ARG 176
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                               3.577 -3.472 2.012 1.00 50.41
            164 CZ ARG 176
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    ATOM
                                2.496 -3.513 1.236 1.00 50.41
            165 NH1 ARG 176
    ATOM
    ATOM
            166 NH2 ARG 176
                                4.536 -4.376 1.841 1.00 50.41
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            167 C ARG 176
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            168 O ARG 176
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                              -0.326 1.935 6.581 1.00 24.74
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                               -1.147 3.145 6.584 1.00 24.74
            170 CA SER 177
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    ATOM
            171 CB SER 177
                               -2.622 2.792 6.414 1.00 21.56
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            173 C SER 177
                              -0.960 4.013 7.832 1.00 24.74
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                              -1.401 5.159 7.863 1.00 21.56
            174 O SER 177
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                              -0.347 3.453 8.870 1.00 17.96
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            175 N THR 178
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            176 CA THR 178
                               -0.104 4.181 10.115 1.00 17.96
                               -0.736 3.440 11.323 1.00 19.76
            177 CB THR 178
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                               -0.265 2.091 11.361 1.00 19.76
            178 OG1 THR 178
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                               -2.253 3.443 11.211 1.00 19.76
            179 CG2 THR 178
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            180 C THR 178
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                               2.207 4.024 9.417 1.00 25.88
            182 N ASN 179
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                               3.654 4.180 9.546 1.00 25.88
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            183 CA ASN 179
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            184 CB ASN 179
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            185 CG ASN 179
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                                6.129 2.768 10.564 1.00 44.29
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            186 OD1 ASN 179
            187 ND2 ASN 179
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                               4.150 5.495 7.590 1.00 44.29
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           189 O ASN 179
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            190 N ALA 180
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            191 CA ALA 180
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            192 CB ALA 180
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                               5.931 7.808 8.170 1.00 45.20
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            193 C ALA 180
            194 O ALA 180
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            196 CA ALA 181
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            199 O ALA 181
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                               8.202 4.769 4.482 1.00 39.06
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	ATOM	205 CA SER 183	9.781 4.270 2.693 1.00 64.55
	ATOM	206 CB SER 183	9.690 3.402 1.430 1.00 67.68
	ATOM	207 OG SER 183	8.822 3.978 0.467 1.00 67.68
	ATOM	208 C SER 183	10.643 5.510 2.437 1.00 64.55
5	ATOM	209 O SER 183	11.839 5.407 2.158 1.00 67.68
	ATOM	210 N HIS 184	10.035 6.683 2.579 1.00 52.73
	ATOM	211 CA HIS 184	10.725 7.953 2.352 1.00 52.73
	ATOM	212 CB HIS 184	9.772 8.955 1.698 1.00 44.77
	ATOM	213 C HIS 184	11.364 8.582 3.595 1.00 52.73
10	ATOM	214 O HIS 184	11.837 9.722 3.540 1.00 44.77
	ATOM	215 N TRP 185	11.420 7.842 4.699 1.00 54.14
	ATOM	216 CA TRP 185	11.977 8.389 5.940 1.00 54.14
	ATOM	217 CB TRP 185	11.813 7.395 7.104 1.00 40.24
	ATOM	218 CG TRP 185	12.605 6.123 6.991 1.00 40.24
15	ATOM	219 CD2 TRP 185	13.894 5.873 7.551 1.00 40.24
	ATOM	220 CE2 TRP 185	14.245 4.543 7.221 1.00 40.24
	ATOM	221 CE3 TRP 185	14.791 6.641 8.300 1.00 40.24
	ATOM	222 CD1 TRP 185	12.227 4.973 6.359 1.00 40.24
	ATOM	223 NE1 TRP 185	13.210 4.015 6.496 1.00 40.24
20	ATOM	224 CZ2 TRP 185	15.461 3.968 7.619 1.00 40.24
	ATOM	225 CZ3 TRP 185	15.996 6.073 8.696 1.00 40.24
	ATOM	226 CH2 TRP 185	16.319 4.747 8.353 1.00 40.24
	ATOM	227 C TRP 185	13.432 8.870 5.819 1.00 54.14
	ATOM	228 O TRP 185	13.759 10.008 6.168 1.00 40.24
25	ATOM	229 N LYS 186	14.277 8.032 5.232 1.00 43.72
	ATOM	230 CA LYS 186	15.694 8.329 5.035 1.00 43.72
	ATOM	231 CB LYS 186	16.353 7.168 4.282 1.00 64.14
	ATOM	232 CG LYS 186	17.830 7.355 3.945 1.00 64.14
	ATOM	233 CD LYS 186	18.758 7.175 5.139 1.00 64.14
30	ATOM	234 CE LYS 186	20.195 7.060 4.652 1.00 64.14
	ATOM	235 NZ LYS 186	20.348 5.838 3.805 1.00 64.14
	ATOM	236 C LYS 186	15.900 9.634 4.263 1.00 43.72
	ATOM	237 O LYS 186	16.948 10.256 4.366 1.00 64.14 14.892 10.032 3.491 1.00 58.06
25	ATOM	238 N GLN 187	•
35	ATOM	239 CA GLN 187	
	ATOM	240 CB GLN 187	14.288 10.997 1.321 1.00 74.68 14.639 9.662 0.667 1.00 74.68
	ATOM	241 CG GLN 187	16.133 9.397 0.607 1.00 74.68
	ATOM	242 CD GLN 187	16.133 9.397 0.007 1.00 74.68
40	ATOM	243 OE1 GLN 187	
40	ATOM	244 NE2 GLN 187	14.322 12.466 3.342 1.00 58.06
	ATOM	245 C GLN 187 246 O GLN 187	14.897 13.551 3.358 1.00 74.68
	ATOM		13.117 12.280 3.866 1.00 54.11
	ATOM		12.363 13.360 4.505 1.00 54.11
45	ATOM	248 CA ARG 188 249 CB ARG 188	10.889 13.115 4.334 1.00 53.33
45	ATOM	250 C ARG 188	12.654 13.626 5.977 1.00 54.11
	ATOM	251 O ARG 188	11.879 14.298 6.659 1.00 53.33
	ATOM	251 O ARG 188 252 N ARG 189	13.754 13.090 6.473 1.00 39.52
	ATOM ATOM	253 CA ARG 189	14.089 13.271 7.875 1.00 39.52
50		254 CB ARG 189	14.594 11.959 8.482 1.00 60.85
50	ATOM	234 CD ARG 169	17.557 11.757 0.702 1.00 00.05

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    ATOM 256 CD ARG 189
                               16,442 10.298 8.693 1.00 60.85
                               17.833 9.963 8.385 1.00 60.85
    ATOM 257 NE ARG 189
    ATOM 258 CZ ARG 189
                               18.627 9.261 9.190 1.00 60.85
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    ATOM 259 NH1 ARG 189
    ATOM 260 NH2 ARG 189
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    ATOM 261 C ARG 189
    ATOM 262 O ARG 189
                              16.037 14.565 7.320 1.00 60.85
    ATOM 263 N LYS 190
                              14.934 15.100 9.212 1.00 44.13
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                              15.068 17.500 9.680 1.00 45.33
    ATOM 265 CB LYS 190
    ATOM 266 C LYS 190
                              16.472 15.846 10.928 1.00 44.13
    ATOM 267 O LYS 190
                              15.827 15.272 11.805 1.00 45.33
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    ATOM 269 CA PHE 191
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                               19.993 16.008 12.025 1.00 53.94
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    ATOM 272 CD1 PHE 191
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    ATOM 273 CD2 PHE 191
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    ATOM 274 CE1 PHE 191
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    ATOM 275 CE2 PHE 191
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                              21.615 12.639 9.900 1.00 53.94
    ATOM 276 CZ PHE 191
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    ATOM 278 O PHE 191
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                               17.683 17.315 15.736 1.00 44.53
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    ATOM 281 CB LEU 192
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                               16.931 17.259 18.246 1.00 22.94
     ATOM 282 CG LEU 192
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     ATOM 283 CD1 LEU 192
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     ATOM 284 CD2 LEU 192
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     ATOM 285 C LEU 192
     ATOM 286 O LEU 192
                              20.049 17.507 16.129 1.00 22.94
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                               17.670 20.241 15.781 1.00 46.23
                               20.058 20.311 16.198 1.00 34.26
     ATOM 289 CA PRO 193
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     ATOM 290 CB PRO 193
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                               18.213 21.641 15.579 1.00 46.23
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                              22.217 19.716 17.125 1.00 42.67
            294 N ASP 194
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                               23.174 19.254 18.128 1.00 42.67
     ATOM 295 CA ASP 194
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            296 CB ASP 194
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                               24.731 18.185 16.450 1.00 68.50
            297 CG ASP 194
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                               25.066 17.027 16.782 1.00 68.50
            298 OD1 ASP 194
     ATOM
            299 OD2 ASP 194
                               24.498 18.518 15.269 1.00 68.50
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                              23.187 20.003 19.457 1.00 42.67
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     ATOM
            301 O ASP 194
                              23.545 19.432 20.486 1.00 68.50
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                              22.817 21.280 19.438 1.00 47.52
            302 N ASP 195
     ATOM
                               22.793 22.070 20.666 1.00 47.52
     ATOM
            303 CA ASP 195
     ATOM 304 CB ASP 195
                               22.586 23.559 20.351 1.00 85.02
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21.327 23.824 19.537 1.00 85.02
             305 CG ASP 195
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             306 OD1 ASP 195
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     ATOM
                                21.377 23.683 18.294 1.00 85.02
             307 OD2 ASP 195
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     ATOM
            308 C ASP 195
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                               21.762 21.826 22.831 1.00 85.02
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            309 O ASP 195
             310 N ILE 196
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            311 CA ILE 196
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            313 CG2 ILE 196
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            315 CD1 ILE 196
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            321 O GLY 197
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            326 O GLN 198
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             330 OG SER 199
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                                22.656 17.108 29.872 1.00 38.71
            334 CD PRO 200
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            336 CB PRO 200
            337 CG PRO 200
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                               19.961 19.041 34.604 1.00 42.94
            341 CA ILE 201
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                               20.059 20.582 34.491 1.00 51.32
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             342 CB ILE 201
                                21.468 20.991 34.078 1.00 51.32
             343 CG2 ILE 201
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     ATOM
             344 CG1 ILE 201
                                19.009 21.111 33.510 1.00 51.32
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             347 O ILE 201
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             349 CA VAL 202
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45
                                15.296 17.722 35.326 1.00 36.59
     ATOM
             350 CB VAL 202
             351 CG1 VAL 202
                                 14.202 17.311 36.304 1.00 36.59
     ATOM
                                 14.968 19.074 34.714 1.00 36.59
     ATOM
             352 CG2 VAL 202
                                17.007 16.435 36.665 1.00 50.33
            353 C VAL 202
     ATOM
                                17.335 15.481 35.955 1.00 36.59
50
     ATOM
            354 O VAL 202
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	ATOM	355 N SER 203	16.960 16.375 37.991 1.00 49.46
	ATOM	356 CA SER 203	17.289 15.166 38.736 1.00 49.46
	ATOM	357 CB SER 203	17.298 15.467 40.241 1.00 64.20
	ATOM	358 OG SER 203	17.673 14.330 41.003 1.00 64.20
5	ATOM	359 C SER 203	16.356 13.992 38.463 1.00 49.46
	ATOM	360 O SER 203	15.147 14.166 38.310 1.00 64.20
	ATOM	361 N MET 204	16.944 12.800 38.419 1.00 41.99
	ATOM	362 CA MET 204	16.223 11.551 38.205 1.00 41.99
	ATOM	363 CB MET 204	16.320 11.096 36.746 1.00 48.64
10	ATOM	364 CG MET 204	15.470 11.895 35.771 1.00 48.64
	ATOM	365 SD MET 204	13.702 11.783 36.114 1.00 48.64
	ATOM	366 CE MET 204	13.284 10.257 35.264 1.00 48.64
	ATOM	367 C MET 204	16.900 10.528 39.109 1.00 41.99
	ATOM	368 O MET 204	18.127 10.417 39.121 1.00 48.64
15	ATOM	369 N PRO 205	16.108 9.754 39.869 1.00 38.42
	ATOM	370 CD PRO 205	14.633 9.815 39.866 1.00 52.20
	ATOM	371 CA PRO 205	16.586 8.724 40.797 1.00 38.42
	ATOM	372 CB PRO 205	15.334 7.888 41.041 1.00 52.20
	ATOM	373 CG PRO 205	14.254 8.919 41.028 1.00 52.20
20	ATOM	374 C PRO 205	17.769 7.858 40.340 1.00 38.42
	ATOM	375 O PRO 205	18.724 7.675 41.092 1.00 52.20
	ATOM	376 N ASP 206	17.720 7.349 39.111 1.00 49.06
	ATOM	377 CA ASP 206	18.791 6.490 38.601 1.00 49.06
	ATOM	378 CB ASP 206	18.282 5.627 37.437 1.00 74.42
25	ATOM	379 CG ASP 206	17.690 6.450 36.305 1.00 74.42
	ATOM	380 OD1 ASP 206	18.397 7.335 35.770 1.00 74.42
	ATOM	381 OD2 ASP 206	16.516 6.199 35.948 1.00 74.42
	ATOM	382 C ASP 206	20.106 7.177 38.214 1.00 49.06
••	ATOM	383 O ASP 206	21.069 6.506 37.838 1.00 74.42
30	ATOM	384 N GLY 207	20.139 8.505 38.272 1.00 42.48
	ATOM	385 CA GLY 207	21.355 9.225 37.928 1.00 42.48 21.330 9.965 36.601 1.00 42.48
	ATOM	386 C GLY 207	21.330 9.965 36.601 1.00 42.48 21.890 11.058 36.494 1.00 42.50
	ATOM	387 O GLY 207 388 N ASP 208	20.725 9.365 35.581 1.00 46.70
25	ATOM	388 N ASP 208 389 CA ASP 208	20.636 9.999 34.266 1.00 46.70
35	ATOM ATOM	390 CB ASP 208	20.162 8.994 33.212 1.00 61.56
	ATOM	391 CG ASP 208	21.143 7.856 33.006 1.00 61.56
	ATOM	391 CO ASI 200 392 OD1 ASP 208	20.723 6.684 33.122 1.00 61.56
	ATOM	393 OD2 ASP 208	22.330 8.134 32.724 1.00 61.56
40	ATOM	394 C ASP 208	19.666 11.176 34.339 1.00 46.70
40	ATOM	395 O ASP 208	18.462 10.983 34.506 1.00 61.56
	ATOM	396 N LYS 209	20.200 12.389 34.238 1.00 41.30
	ATOM	397 CA LYS 209	19.389 13.602 34.308 1.00 41.30
	ATOM	398 CB LYS 209	20.254 14.782 34.732 1.00 41.38
45	ATOM	399 C LYS 209	18.657 13.916 33.004 1.00 41.30
, ,	ATOM	400 O LYS 209	19.052 13.458 31.930 1.00 41.38
	ATOM	401 N VAL 210	17.603 14.723 33.109 1.00 43.36
	ATOM	402 CA VAL 210	16.792 15.107 31.954 1.00 43.36
	ATOM	403 CB VAL 210	15.275 15.014 32.282 1.00 30.23
50	ATOM	404 CG1 VAL 210	14.440 15.358 31.055 1.00 30.23

	4 TO 8 4	405 CG2 VAL 210	14.923 13.624 32.782 1.00 30.23
	ATOM ATOM	406 C VAL 210	17.088 16.522 31.442 1.00 43.36
	ATOM	407 O VAL 210	17.395 17.430 32.221 1.00 30.23
	ATOM	407 O VAL 210 408 N ASP 211	17.004 16.685 30.125 1.00 27.49
=	ATOM	409 CA ASP 211	17.217 17.966 29.458 1.00 27.49
5		410 CB ASP 211	18.073 17.765 28.198 1.00 30.75
	ATOM ATOM	411 CG ASP 211	18.360 19.068 27.447 1.00 30.75
	ATOM	412 OD1 ASP 211	19.473 19.196 26.900 1.00 30.75
	ATOM	412 OD1 ASP 211 413 OD2 ASP 211	17.484 19.955 27.370 1.00 30.75
10	ATOM	414 C ASP 211	15.819 18.445 29.073 1.00 27.49
10	ATOM	414 C ASP 211 415 O ASP 211	15.197 17.892 28.166 1.00 30.75
			15.343 19.488 29.745 1.00 31.99
	ATOM	416 N LEU 212 417 CA LEU 212	14.013 20.042 29.492 1.00 31.99
	ATOM	417 CA LEU 212 418 CB LEU 212	13.778 21.274 30.369 1.00 35.19
1.5	ATOM	418 CB LEU 212 419 CG LEU 212	13.606 20.997 31.864 1.00 35.19
15	ATOM	419 CO LEU 212 420 CD1 LEU 212	13.621 22.298 32.652 1.00 35.19
	ATOM		12.309 20.237 32.098 1.00 35.19
	ATOM		13.713 20.377 28.032 1.00 31.99
	ATOM		12.625 20.083 27.539 1.00 35.19
20	ATOM ATOM	423 O LEU 212 424 N GLU 213	14.672 20.981 27.338 1.00 28.70
20	ATOM	424 N GLU 213 425 CA GLU 213	14.468 21.345 25.940 1.00 28.70
	ATOM	426 CB GLU 213	15.623 22.209 25.428 1.00 62.21
	ATOM	420 CB GLU 213	15.434 22.707 23.997 1.00 62.21
	ATOM	427 CG GLO 213 428 CD GLU 213	16.651 23.440 23.446 1.00 62.21
25	ATOM	429 OE1 GLU 213	17.778 23.214 23.945 1.00 62.21
23	ATOM	430 OE2 GLU 213	16.478 24.237 22.498 1.00 62.21
	ATOM	430 OE2 GLO 213	14.317 20.104 25.067 1.00 28.70
	ATOM	431 C GLO 213 432 O GLU 213	13.403 20.024 24.247 1.00 62.21
	ATOM	432 O GLO 213 433 N ALA 214	15.201 19.130 25.262 1.00 28.17
30	ATOM	434 CA ALA 214	15.162 17.890 24.494 1.00 28.17
50	ATOM	435 CB ALA 214	16.330 16.998 24.872 1.00 42.74
	ATOM	436 C ALA 214	13.844 17.176 24.759 1.00 28.17
	ATOM	437 O ALA 214	13.174 16.726 23.829 1.00 42.74
	ATOM	438 N PHE 215	13.468 17.104 26.032 1.00 21.66
35	ATOM	439 CA PHE 215	12.222 16.471 26.444 1.00 21.66
55	ATOM	440 CB PHE 215	12.033 16.628 27.958 1.00 28.76
	ATOM	441 CG PHE 215	10.751 16.038 28.481 1.00 28.76
	ATOM	442 CD1 PHE 215	10.675 14.689 28.815 1.00 28.76
	ATOM		9.623 16.835 28.653 1.00 28.76
40	ATOM	444 CE1 PHE 215	9.493 14.143 29.315 1.00 28.76
40	ATOM	445 CE2 PHE 215	8.438 16.300 29.150 1.00 28.76
	ATOM	446 CZ PHE 215	8.373 14.951 29.482 1.00 28.76
	ATOM	447 C PHE 215	11.068 17.132 25.696 1.00 21.66
	ATOM	448 O PHE 215	10.215 16.451 25.122 1.00 28.76
45	ATOM		11.073 18.462 25.680 1.00 28.03
.,	ATOM	450 CA SER 216	10.043 19.242 25.007 1.00 28.03
	ATOM		10.349 20.734 25.146 1.00 33.85
	ATOM		9.300 21.529 24.624 1.00 33.85
	ATOM	453 C SER 216	9.945 18.857 23.532 1.00 28.03
50	ATOM	454 O SER 216	8.852 18.613 23.019 1.00 33.85
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	ATOM	455 N GLU 217	11.092 18.761 22.868 1.00 28.84 11.138 18.402 21.454 1.00 28.84
	ATOM	456 CA GLU 217	12.581 18.420 20.943 1.00 47.68
	ATOM	457 CB GLU 217	13.174 19.815 20.811 1.00 47.68
_	ATOM	458 CG GLU 217 459 CD GLU 217	12.405 20.684 19.829 1.00 47.68
5	ATOM	459 CD GLU 217 460 OE1 GLU 217	11.660 21.581 20.281 1.00 47.68
	ATOM		12.542 20.465 18.606 1.00 47.68
	ATOM	461 OE2 GLU 217 462 C GLU 217	10.505 17.044 21.179 1.00 28.84
	ATOM	462 C GLU 217 463 O GLU 217	9.751 16.886 20.217 1.00 47.68
10	ATOM	464 N PHE 218	10.799 16.071 22.036 1.00 21.49
10	ATOM ATOM	465 CA PHE 218	10.259 14.725 21.883 1.00 21.49
	ATOM	466 CB PHE 218	11.020 13.746 22.781 1.00 24.12
	ATOM	467 CG PHE 218	12.489 13.652 22.464 1.00 24.12
	ATOM	468 CD1 PHE 218	13.431 13.554 23.481 1.00 24.12
15	ATOM	469 CD2 PHE 218	12.932 13.677 21.144 1.00 24.12
15	ATOM	470 CE1 PHE 218	14.793 13.484 23.187 1.00 24.12
	ATOM	470 CETTTLE 218	14.290 13.607 20.843 1.00 24.12
	ATOM	471 CE211E 218	15.221 13.511 21.867 1.00 24.12
	ATOM	473 C PHE 218	8.765 14.675 22.176 1.00 21.49
20	ATOM	474 O PHE 218	7.985 14.166 21.369 1.00 24.12
20	ATOM	475 N THR 219	8.358 15.227 23.312 1.00 20.07
	ATOM	476 CA THR 219	6.949 15.231 23.685 1.00 20.07
	ATOM	477 CB THR 219	6.741 15.766 25.118 1.00 28.98
	ATOM	478 OG1 THR 219	7.418 17.021 25.274 1.00 28.98
25	ATOM	479 CG2 THR 219	7.275 14.767 26.132 1.00 28.98
	ATOM	480 C THR 219	6.080 16.011 22.696 1.00 20.07
	ATOM	481 O THR 219	4.914 15.670 22.482 1.00 28.98
	ATOM	482 N LYS 220	6.662 17.022 22.060 1.00 25.35
	ATOM	483 CA LYS 220	5.943 17.840 21.088 1.00 25.35
30	ATOM	484 CB LYS 220	6.842 18.965 20.577 1.00 29.07
	ATOM	485 C LYS 220	5.414 17.015 19.916 1.00 25.35
	ATOM	486 O LYS 220	4.376 17.343 19.339 1.00 29.07
	ATOM	487 N ILE 221	6.122 15.943 19.569 1.00 31.43
	ATOM	488 CA ILE 221	5.708 15.089 18.458 1.00 31.43
35	ATOM	489 CB ILE 221	6.842 14.915 17.413 1.00 25.19
	ATOM	490 CG2 ILE 221	7.240 16.264 16.838 1.00 25.19
	ATOM	491 CG1 ILE 221	8.050 14.215 18.043 1.00 25.19
	ATOM	492 CD1 ILE 221	9.113 13.799 17.044 1.00 25.19
	ATOM	493 C ILE 221	5.240 13.700 18.892 1.00 31.43
40	ATOM	494 O ILE 221	4.930 12.857 18.046 1.00 25.19
	ATOM	495 N ILE 222	5.129 13.474 20.198 1.00 24.41
	ATOM	496 CA ILE 222	4.720 12.162 20.687 1.00 24.41
	ATOM	497 CB ILE 222	5.189 11.916 22.147 1.00 27.10
	ATOM	498 CG2 ILE 222	4.221 12.545 23.145 1.00 27.10
45	ATOM	499 CG1 ILE 222	5.302 10.410 22.400 1.00 27.10
	ATOM	500 CD1 ILE 222	6.062 10.053 23.646 1.00 27.10
	ATOM	501 C ILE 222	3.231 11.845 20.541 1.00 24.41
	ATOM	502 O ILE 222	2.864 10.691 20.307 1.00 27.10
50	ATOM	503 N THR 223	2.378 12.861 20.642 1.00 33.16 0.936 12.653 20.520 1.00 33.16
50	ATOM	504 CA THR 223	0.930 12.033 20.320 1.00 33.10

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505 CB THR 223
                               0.150 13.974 20.721 1.00 36.84
    ATOM
                                0.352 14.442 22.063 1.00 36.84
    ATOM
            506 OG1 THR 223
                               -1.346 13.764 20.484 1.00 36.84
            507 CG2 THR 223
    ATOM
            508 C THR 223
                              0.536 11.954 19.212 1.00 33.16
    ATOM
                              -0.156 10.932 19.242 1.00 36.84
    ATOM 509 O THR 223
    ATOM 510 N PRO 224
                              0.968 12.482 18.048 1.00 18.75
                               1.691 13.735 17.770 1.00 26.12
            511 CD PRO 224
    ATOM
                               0.590 11.805 16.802 1.00 18.75
           512 CA PRO 224
    ATOM
                               1.117 12.747 15.715 1.00 26.12
    ATOM 513 CB PRO 224
    ATOM 514 CG PRO 224
                               2.221 13.497 16.386 1.00 26.12
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    ATOM 515 C PRO 224
                              1.200 10.402 16.701 1.00 18.75
                              0.606 9.502 16.101 1.00 26.12
    ATOM 516 O PRO 224
    ATOM 517 N ALA 225
                              2.368 10.213 17.312 1.00 12.19
                               3.040 8.916 17.300 1.00 12.19
           518 CA ALA 225
    ATOM
           519 CB ALA 225
                               4.415 9.021 17.943 1.00 20.39
    ATOM
15
    ATOM 520 C ALA 225
                              2.187 7.881 18.030 1.00 12.19
    ATOM 521 O ALA 225
                              1.998 6.764 17.545 1.00 20.39
                              1.645 8.271 19.179 1.00 14.61
    ATOM
           522 N ILE 226
    ATOM 523 CA ILE 226
                              0.798 7.385 19.971 1.00 14.61
    ATOM 524 CB ILE 226
                              0.450 8.025 21.332 1.00 16.10
20
                              -0.508 7.132 22.108 1.00 16.10
           525 CG2 ILE 226
    ATOM
                               1.729 8.293 22.132 1.00 16.10
           526 CG1 ILE 226
    ATOM
    ATOM 527 CD1 ILE 226
                               1.509 9.113 23.387 1.00 16.10
    ATOM 528 C ILE 226
                             -0.499 7.094 19.213 1.00 14.61
                             -0.986 5.961 19.200 1.00 16.10
    ATOM 529 O ILE 226
25
                              -1.042 8.123 18.569 1.00 15.93
           530 N THR 227
    ATOM
           531 CA THR 227
                               -2.278 7.997 17.800 1.00 15.93
    ATOM
                               -2.706 9.360 17.207 1.00 22.37
    ATOM
           532 CB THR 227
           533 OG1 THR 227
                               -2.890 10.301 18.273 1.00 22.37
    ATOM
                               -4.014 9.232 16.434 1.00 22.37
    ATOM 534 CG2 THR 227
30
                              -2.149 6.964 16.680 1.00 15.93
    ATOM 535 C THR 227
                              -3.091 6.217 16.402 1.00 22.37
    ATOM
           536 O THR 227
            537 N ARG 228
                              -0.982 6.916 16.045 1.00 14.49
    ATOM
                               -0.750 5.956 14.975 1.00 14.49
    ATOM
            538 CA ARG 228
           539 CB ARG 228
                                0.602 6.188 14.307 1.00 33.87
    ATOM
35
                                0.701 7.482 13.540 1.00 33.87
           540 CG ARG 228
    ATOM
                                2.053 7.572 12.868 1.00 33.87
    ATOM 541 CD ARG 228
    ATOM 542 NE ARG 228
                                2.510 8.952 12.793 1.00 33.87
                               3.551 9.431 13.469 1.00 33.87
           543 CZ ARG 228
    ATOM
                                4,256 8.634 14.270 1.00 33.87
           544 NH1 ARG 228
40
    ATOM
                                3.864 10.716 13.374 1.00 33.87
    ATOM
           545 NH2 ARG 228
                              -0.813 4.531 15.516 1.00 14.49
    ATOM 546 C ARG 228
                              -1.309 3.632 14.839 1.00 33.87
     ATOM
           547 O ARG 228
                              -0.313 4.327 16.735 1.00 14.80
    ATOM 548 N VAL 229
                               -0.333 3.002 17.352 1.00 14.80
     ATOM 549 CA VAL 229
45
    ATOM 550 CB VAL 229
                                0.456 2.979 18.683 1.00 13.78
                                0.339 1.612 19.350 1.00 13.78
    ATOM 551 CG1 VAL 229
     ATOM 552 CG2 VAL 229
                                1.915 3.312 18.430 1.00 13.78
                              -1.788 2.602 17.591 1.00 14.80
     ATOM 553 C VAL 229
                              -2.185 1.465 17.323 1.00 13.78
    ATOM 554 O VAL 229
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-2.588 3.561 18.047 1.00 9.33
     ATOM 555 N VAL 230
                               -4.005 3.327 18.292 1.00 9.33
    ATOM 556 CA VAL 230
                               -4.679 4.564 18.909 1.00 16.07
    ATOM 557 CB VAL 230
    ATOM 558 CG1 VAL 230
                                -6.168 4.319 19.076 1.00 16.07
                                -4.038 4.896 20.253 1.00 16.07
    ATOM 559 CG2 VAL 230
                               -4.700 2.982 16.981 1.00 9.33
     ATOM 560 C VAL 230
                               -5,504 2,049 16,929 1,00 16,07
            561 O VAL 230
     ATOM
                              -4.364 3.719 15.922 1.00 12.71
            562 N ASP 231
     ATOM
                               -4.951 3.496 14.603 1.00 12.71
     ATOM 563 CA ASP 231
     ATOM 564 CB ASP 231
                               -4.529 4.596 13.624 1.00 27.08
10
                               -5.053 5.967 14.020 1.00 27.08
     ATOM 565 CG ASP 231
                                -6.144 6.047 14.624 1.00 27.08
     ATOM
            566 OD1 ASP 231
                                -4.370 6.969 13.723 1.00 27.08
            567 OD2 ASP 231
     ATOM
     ATOM 568 C ASP 231
                              -4.570 2.132 14.049 1.00 12.71
                              -5.413 1.436 13.483 1.00 27.08
     ATOM 569 O ASP 231
15
                              -3.305 1.755 14.215 1.00 14.33
     ATOM 570 N PHE 232
                               -2.823 0.461 13.748 1.00 14.33
     ATOM 571 CA PHE 232
     ATOM 572 CB PHE 232
                               -1.351 0.257 14.134 1.00 16.35
     ATOM 573 CG PHE 232
                               -0.911 -1.184 14.097 1.00 16.35
     ATOM 574 CD1 PHE 232
                                -0.789 -1.862 12.887 1.00 16.35
20
            575 CD2 PHE 232
                                -0.661 -1.879 15.280 1.00 16.35
     ATOM
                                -0.430 -3.208 12.851 1.00 16.35
     ATOM
            576 CE1 PHE 232
     ATOM 577 CE2 PHE 232
                                -0.302 -3.224 15.255 1.00 16.35
     ATOM 578 CZ PHE 232
                               -0.187 -3.890 14.038 1.00 16.35
                               -3.670 -0.642 14.368 1.00 14.33
            579 C PHE 232
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     ATOM
                               -4.226 -1.482 13.661 1.00 16.35
     ATOM 580 O PHE 232
     ATOM
            581 N ALA 233
                               -3.769 -0.619 15.695 1.00 15.30
            582 CA ALA 233
                                -4.537 -1.607 16.444 1.00 15.30
     ATOM
                                -4.413 -1.335 17.938 1.00 12.88
            583 CB ALA 233
     ATOM
                               -6.005 -1.609 16.030 1.00 15.30
     ATOM 584 C ALA 233
30
                               -6.627 -2.663 15.902 1.00 12.88
     ATOM
            585 O ALA 233
            586 N LYS 234
                               -6.542 -0.419 15.795 1.00 25.69
     ATOM
            587 CA LYS 234
                               -7.933 -0.256 15.401 1.00 25.69
     ATOM
            588 CB LYS 234
                               -8.270 1.234 15.318 1.00 45.91
     ATOM
                               -9.574 1.595 15.979 1.00 45.91
            589 CG LYS 234
35
     ATOM
                               -9.535 1.268 17.463 1.00 45.91
            590 CD LYS 234
     ATOM
                               -10.938 1.047 18.006 1.00 45.91
     ATOM
            591 CE LYS 234
                               -11.605 -0.106 17.327 1.00 45.91
     ATOM
            592 NZ LYS 234
                               -8.240 -0.931 14.067 1.00 25.69
            593 C LYS 234
     ATOM
                               -9.368 -1.368 13.827 1.00 45.91
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     ATOM
            594 O LYS 234
            595 N LYS 235
                               -7.234 -1.019 13.204 1.00 17.44
     ATOM
                               -7.406 -1.627 11.892 1.00 17.44
            596 CA LYS 235
     ATOM
                               -6.459 -0.975 10.884 1.00 26.26
     ATOM
            597 CB LYS 235
                                -6.757 0.499 10.669 1.00 26.26
     ATOM
            598 CG LYS 235
                               -5.785 1.141 9.706 1.00 26.26
            599 CD LYS 235
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     ATOM
            600 CE LYS 235
                               -6.154 2.593 9.460 1.00 26.26
     ATOM
                               -5.231 3.230 8.484 1.00 26.26
            601 NZ LYS 235
     ATOM
            602 C LYS 235
                               -7.258 -3.146 11.875 1.00 17.44
     ATOM
                               -7.365 -3.773 10.817 1.00 26.26
            603 O LYS 235
     ATOM
                               -7.015 -3.738 13.040 1.00 21.99
     ATOM 604 N LEU 236
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-6.880 -5.187 13.144 1.00 21.99
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            606 CB LEU 236
    ATOM
                               -4.362 -5.127 13.818 1.00 25.38
    ATOM
            607 CG LEU 236
                                -3.415 -5.555 14.929 1.00 25.38
            608 CD1 LEU 236
    ATOM
                                -3.931 -5.725 12.491 1.00 25.38
            609 CD2 LEU 236
    ATOM
                               -8.219 -5.796 13.556 1.00 21.99
    ATOM
            610 C LEU 236
            611 O LEU 236
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    ATOM
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    ATOM 612 N PRO 237
                               -7.936 -7.474 11.730 1.00 42.99
    ATOM 613 CD PRO 237
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            614 CA PRO 237
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    ATOM
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    ATOM 615 CB PRO 237
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    ATOM 616 CG PRO 237
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    ATOM 617 C PRO 237
                              -11.142 -7.563 15.159 1.00 42.99
     ATOM 618 O PRO 237
                               -9.301 -8.843 15.021 1.00 40.45
    ATOM 619 N MET 238
15
    ATOM 620 CA MET 238
                                -9.433 -9.364 16.382 1.00 40.45
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     ATOM 622 CG MET 238
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             648 OE1 GLU 241
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             649 OE2 GLU 241
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     ATOM
            654 CB LEU 242 -11.352 -6.473 22.412 1.00 19.79
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            657 CD2 LEU 242
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            659 O LEU 242
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            663 CB PRO 243
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            684 CB ASP 246
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             687 OD2 ASP 246
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            693 CG GLN 247
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             695 OE1 GLN 247
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             696 NE2 GLN 247
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             698 O GLN 247
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     ATOM
             699 N ILE 248
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             700 CA ILE 248
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             701 CB ILE 248
                               -8.238 1.137 27.410 1.00 24.32
     ATOM
                                -7.385 2.055 28.282 1.00 24.32
             702 CG2 ILE 248
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             703 CG1 ILE 248
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            708 CA ILE 249
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            709 CB ILE 249
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            717 CB LEU 250
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            718 CG LEU 250
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            726 CG LEU 251
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            727 CD1 LEU 251
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            731 N LYS 252
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            732 CA LYS 252
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            739 O LYS 252
            740 N GLY 253
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     ATOM
            741 CA GLY 253
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     ATOM
            742 C GLY 253
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            743 O GLY 253
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            745 CA CYS 254
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            746 CB CYS 254
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     ATOM
            747 SG CYS 254
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            748 C CYS 254
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     ATOM
            749 O CYS 254
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                               2.004 0.193 23.724 1.00 14.98
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            750 N CYS 255
            751 CA CYS 255
                                2.309 1.461 23.066 1.00 14.98
     ATOM
                                1.611 2.616 23.781 1.00 24.32
     ATOM
            752 CB CYS 255
            753 SG CYS 255
                                1.602 4.153 22.841 1.00 24.32
     ATOM
                               3,804 1.750 22.922 1.00 14.98
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     ATOM 754 C CYS 255
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	ATOM	755 O CYS 255	4.305 1.895 21.805 1.00 24.32
	ATOM	756 N MET 256	4.525 1.777 24.037 1.00 13.77
	ATOM	757 CA MET 256	5.959 2.056 24.003 1.00 13.77
	ATOM	757 CA MET 250 758 CB MET 256	6.515 2.218 25.423 1.00 19.23
5	ATOM	750 CB MET 250 759 CG MET 256	7.988 2.607 25.477 1.00 19.23
,	ATOM	760 SD MET 256	8.344 4.132 24.571 1.00 19.23
	ATOM	761 CE MET 256	10.127 4.254 24.782 1.00 19.23
	ATOM	762 C MET 256	6.734 0.978 23.246 1.00 13.77
	ATOM	763 O MET 256	7.672 1.284 22.516 1.00 19.23
10	ATOM	764 N GLU 257	6.316 -0.275 23.400 1.00 12.57
10	ATOM	765 CA GLU 257	6.971 -1.397 22.730 1.00 12.57
	ATOM	766 CB GLU 257	6.342 -2.716 23.182 1.00 31.54
	ATOM	767 CG GLU 257	6.497 -2.982 24.677 1.00 31.54
	ATOM	768 CD GLU 257	5.720 -4.196 25.167 1.00 31.54
15	ATOM	769 OEI GLU 257	5.220 -4.983 24.334 1.00 31.54
13	ATOM	770 OE2 GLU 257	5.607 -4.361 26.400 1.00 31.54
	ATOM	771 C GLU 257	6.889 -1.254 21.211 1.00 12.57
	ATOM	772 O GLU 257	7.881 -1.452 20.505 1.00 31.54
	ATOM	772 O GEO 257 773 N ILE 258	5.712 -0.881 20.717 1.00 17.89
20	ATOM	774 CA ILE 258	5.508 -0.692 19.288 1.00 17.89
	ATOM	775 CB ILE 258	4.001 -0.555 18.946 1.00 15.57
	ATOM	776 CG2 ILE 258	3.813 -0.129 17.493 1.00 15.57
	ATOM	777 CG1 ILE 258	3.288 -1.886 19.211 1.00 15.57
	ATOM	778 CD1 ILE 258	1.798 -1.872 18.922 1.00 15.57
25	ATOM	779 C ILE 258	6.289 0.535 18.811 1.00 17.89
	ATOM	780 O ILE 258	7.000 0.468 17.805 1.00 15.57
	ATOM	781 N MET 259	6.196 1.636 19.556 1.00 11.23
	ATOM	782 CA MET 259	6.907 2.861 19.201 1.00 11.23
	ATOM	783 CB MET 259	6.568 3.995 20.175 1.00 22.19
30	ATOM	784 CG MET 259	5.112 4.439 20.117 1.00 22.19
	ATOM	785 SD MET 259	4.828 6.033 20.915 1.00 22.19
	ATOM	786 CE MET 259	5.038 5.606 22.621 1.00 22.19
	ATOM	787 C MET 259	8.415 2.637 19.131 1.00 11.23
	ATOM	788 O MET 259	9.060 3.008 18.145 1.00 22.19
35	ATOM	789 N SER 260	8.974 1.994 20.153 1.00 8.59
	ATOM	790 CA SER 260	10.408 1.706 20.195 1.00 8.59
	ATOM	791 CB SER 260	10.763 0.939 21.472 1.00 23.39
	ATOM	792 OG SER 260	10.430 1.685 22.623 1.00 23.39
	ATOM	793 C SER 260	10.793 0.864 18.977 1.00 8.59
40	ATOM	794 O SER 260	11.824 1.100 18.350 1.00 23.39
	ATOM	795 N LEU 261	9.952 -0.111 18.644 1.00 13.26
	ATOM	796 CA LEU 261	10.194 -0.992 17.507 1.00 13.26
	ATOM	797 CB LEU 261	9.076 -2.035 17.401 1.00 14.32
	ATOM	798 CG LEU 261	9.019 -2.894 16.134 1.00 14.32
45	ATOM	799 CD1 LEU 261	10.278 -3.733 15.999 1.00 14.32
	ATOM	800 CD2 LEU 261	7.785 -3.772 16.174 1.00 14.32
	ATOM	801 C LEU 261	10.276 -0.170 16.220 1.00 13.26
	ATOM	802 O LEU 261	11.213 -0.313 15.432 1.00 14.32
	ATOM	803 N ARG 262	9.330 0.744 16.043 1.00 10.57
50	ATOM	804 CA ARG 262	9.278 1.598 14.861 1.00 10.57

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	ATOM	805 CB ARG 262	8.018 2.454 14.917 1.00 16.08
	ATOM	806 CG ARG 262	6.755 1.647 14.728 1.00 16.08
	ATOM	807 CD ARG 262	5.540 2.525 14.614 1.00 16.08
	ATOM	808 NE ARG 262	4.418 1.765 14.076 1.00 16.08
5	ATOM	809 CZ ARG 262	3.260 2.289 13.689 1.00 16.08
	ATOM	810 NH1 ARG 262	3.050 3.596 13.780 1.00 16.08
	ATOM	811 NH2 ARG 262	2.322 1.497 13.183 1.00 16.08
	ATOM	812 C ARG 262	10.530 2.471 14.704 1.00 10.57
	ATOM	813 O ARG 262	11.038 2.649 13.589 1.00 16.08
10	ATOM	814 N ALA 263	11.016 3.014 15.820 1.00 13.37
	ATOM	815 CA ALA 263	12.221 3.842 15.831 1.00 13.37
	ATOM	816 CB ALA 263	12.363 4.516 17.172 1.00 17.12
	ATOM	817 C ALA 263	13.443 2.964 15.561 1.00 13.37
	ATOM	818 O ALA 263	14.313 3.316 14.762 1.00 17.12
15	ATOM	819 N ALA 264	13.474 1.802 16.207 1.00 16.55
13	ATOM	820 CA ALA 264	14.574 0.855 16.072 1.00 16.55
	ATOM	821 CB ALA 264	14.375 -0.327 17.019 1.00 24.62
	ATOM	821 CB ALA 204 822 C ALA 264	14.770 0.364 14.642 1.00 16.55
	ATOM	823 O ALA 264	15.904 0.244 14.169 1.00 24.62
20		824 N VAL 265	13.670 0.073 13.955 1.00 22.25
20	ATOM		13.754 -0.401 12.583 1.00 22.25
	ATOM		12.428 -1.038 12.086 1.00 25.31
	ATOM	826 CB VAL 265	12.079 -2.239 12.936 1.00 25.31
	ATOM	827 CG1 VAL 265	11.302 -0.030 12.091 1.00 25.31
	ATOM	828 CG2 VAL 265	
25	ATOM	829 C VAL 265	
	ATOM	830 O VAL 265	14.615 0.434 10.513 1.00 25.31
	ATOM	831 N ARG 266	14.124 1.955 12.092 1.00 26.45
	ATOM	832 CA ARG 266	14.567 3.086 11.283 1.00 26.45
	ATOM	833 CB ARG 266	13.596 4.261 11.399 1.00 38.04
30	ATOM	834 CG ARG 266	12.232 4.019 10.807 1.00 38.04
	ATOM	835 CD ARG 266	11.503 5.339 10.651 1.00 38.04
	ATOM	836 NE ARG 266	10.074 5.216 10.925 1.00 38.04
	ATOM	837 CZ ARG 266	9.504 5.551 12.079 1.00 38.04
	ATOM	838 NH1 ARG 266	10.237 6.038 13.075 1.00 38.04
35	ATOM	839 NH2 ARG 266	8.196 5.411 12.240 1.00 38.04
	ATOM	840 C ARG 266	15.957 3.531 11.729 1.00 26.45
	ATOM	841 O ARG 266	16.296 4.717 11.660 1.00 38.04
	ATOM	842 N TYR 267	16.733 2.590 12.251 1.00 24.87
	ATOM	843 CA TYR 267	18.083 2.888 12.700 1.00 24.87
40	ATOM	844 CB TYR 267	18.592 1.788 13.639 1.00 25.84
	ATOM	845 CG TYR 267	20.073 1.865 13.931 1.00 25.84
	ATOM	846 CD1 TYR 267	20.579 2.789 14.844 1.00 25.84
	ATOM	847 CE1 TYR 267	21.940 2.865 15.103 1.00 25.84
	ATOM	848 CD2 TYR 267	20.971 1.017 13.284 1.00 25.84
45	ATOM	849 CE2 TYR 267	22.331 1.085 13.536 1.00 25.84
-	ATOM	850 CZ TYR 267	22.810 2.011 14.444 1.00 25.84
	ATOM	851 OH TYR 267	24.162 2.078 14.683 1.00 25.84
	ATOM	852 C TYR 267	18.999 3.009 11.488 1.00 24.87
	ATOM	853 O TYR 267	19.019 2.130 10.625 1.00 25.84
50	ATOM	854 N ASP 268	19.751 4.102 11.423 1.00 28.13
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855 CA ASP 268
                               20.666 4.320 10.313 1.00 28.13
    ATOM
    ATOM
            856 CB ASP 268
                               20.524 5.744 9.773 1.00 51.63
            857 CG ASP 268
                               21.339 5.973 8.517 1.00 51.63
    ATOM
                               21.060 5.305 7.498 1.00 51.63
    ATOM
            858 OD1 ASP 268
            859 OD2 ASP 268
                               22,262 6.814 8.547 1.00 51.63
    ATOM
            860 C ASP 268
                              22.105 4.068 10.749 1.00 28.13
    ATOM
                              22.683 4.854 11.500 1.00 51.63
    ATOM
            861 O ASP 268
            862 N PRO 269
                              22.707 2.964 10.276 1.00 37.07
    ATOM
    ATOM 863 CD PRO 269
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            864 CA PRO 269
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            865 CB PRO 269
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    ATOM
    ATOM
            866 CG PRO 269
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            867 C PRO 269
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            868 O PRO 269
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            870 CA ALA 270
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            871 CB ALA 270
            872 C ALA 270
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            873 O ALA 270
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                              24.899 7.081 10.009 1.00 34.54
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    ATOM
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    ATOM
            876 CB SER 271
                               23.959 9.259 10.618 1.00 42.29
    ATOM 877 OG SER 271
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                              25.169 8.607 13.297 1.00 42.29
    ATOM
            879 O SER 271
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            882 CB ASP 272
                               25.720 6.078 14.772 1.00 47.32
    ATOM
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            891 OG1 THR 273
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    ATOM
            892 CG2 THR 273
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                              19.701 6.829 14.442 1.00 27.60
            893 C THR 273
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    ATOM
            894 O THR 273
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                              18.696 7.192 15.232 1.00 20.89
            895 N LEU 274
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                               17.374 6.574 15.161 1.00 20.89
            896 CA LEU 274
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                               16.862 6.193 16.555 1.00 22.48
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     ATOM
                               17.480 5.009 17.301 1.00 22.48
     ATOM
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            913 CG LEU 276
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            914 CD1 LEU 276
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    ATOM
            915 CD2 LEU 276
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    ATOM
            917 O LEU 276
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    ATOM
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            919 CA SER 277
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    ATOM
            920 CB SER 277
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    ATOM
    ATOM 921 OG SER 277
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            922 C SER 277
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            923 O SER 277
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            926 C GLY 278
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    ATOM
                               10.516 10.725 8.631 1.00 44.04
            927 O GLY 278
    ATOM
    ATOM
            928 N GLU 279
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    ATOM
            929 CA GLU 279
                                11.056 12.717 10.479 1.00 37.82
                                9.808 13.600 10.612 1.00 70.24
    ATOM
            930 CB GLU 279
           931 CG GLU 279
                                9.202 13.631 12.014 1.00 70.24
    ATOM
            932 CD GLU 279
                                8.028 14.593 12.141 1.00 70.24
    ATOM
    ATOM
            933 OE1 GLU 279
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            934 OE2 GLU 279
                                7.103 14.535 11.301 1.00 70.24
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           935 C GLU 279
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    ATOM
            936 O GLU 279
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    ATOM
                               12.424 12.811 12.505 1.00 33.77
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            937 N MET 280
    ATOM
            938 CA MET 280
                               13.482 13.360 13.344 1.00 33.77
            939 CB MET 280
                                12.903 13.848 14.674 1.00 33.89
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    ATOM
                                13.898 14.595 15.545 1.00 33.89
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            940 CG MET 280
                               13.350 14.740 17.256 1.00 33.89
            941 SD MET 280
    ATOM
    ATOM
            942 CE MET 280
                               12.100 16.017 17.121 1.00 33.89
                               14.620 12.383 13.613 1.00 33.77
    ATOM
            943 C MET 280
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            944 O MET 280
                               14.432 11.366 14.282 1.00 33.89
    ATOM
                               15.797 12.690 13.080 1.00 30.24
    ATOM
            945 N ALA 281
                                16.972 11.852 13.287 1.00 30.24
    ATOM
            946 CA ALA 281
                               17.937 11.998 12.120 1.00 25.10
    ATOM
            947 CB ALA 281
    ATOM
            948 C ALA 281
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    ATOM
            949 O ALA 281
                               17.743 11.401 15.551 1.00 32.12
    ATOM
            950 N VAL 282
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    ATOM
            951 CA VAL 282
                                17.303 11.606 17.991 1.00 37.75
     ATOM
            952 CB VAL 282
                                16.184 12.615 17.799 1.00 37.75
     ATOM
            953 CG1 VAL 282
     ATOM 954 CG2 VAL 282
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955 C VAL 282
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    ATOM
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    ATOM
            958 CA LYS 283
                               21.700 10.722 18.328 1.00 26.82
    ATOM
            959 CB LYS 283
                               22.894 11.679 18.342 1.00 57.25
    ATOM
            960 CG LYS 283
                               23.258 12.245 16.979 1.00 57.25
    ATOM
                               24.282 13.361 17.105 1.00 57.25
    ATOM
            961 CD LYS 283
    ATOM 962 CE LYS 283
                               24.752 13.836 15.741 1.00 57.25
    ATOM 963 NZ LYS 283
                               25.518 12.772 15.033 1.00 57.25
                              21.509 10.120 19.717 1.00 26.82
    ATOM 964 C LYS 283
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            965 O LYS 283
                              20.648 10.566 20.477 1.00 57.25
    ATOM
            966 N ARG 284
    ATOM
                              22.351 9.146 20.058 1.00 26.41
                               22.297 8.457 21.351 1.00 26.41
    ATOM
            967 CA ARG 284
    ATOM 968 CB ARG 284
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                               23.715 6.539 20.440 1.00 41.02
            969 CG ARG 284
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    ATOM
                               25.016 5.794 20.616 1.00 41.02
           970 CD ARG 284
    ATOM
    ATOM
            971 NE ARG 284
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    ATOM
            972 CZ ARG 284
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    ATOM
            973 NH1 ARG 284
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            974 NH2 ARG 284
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            975 C ARG 284
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    ATOM
    ATOM
            976 O ARG 284
                              21.296 9.278 23.370 1.00 41.02
    ATOM
            977 N GLU 285
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    ATOM 978 CA GLU 285
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    ATOM
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            980 CG GLU 285
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            981 CD GLU 285
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            982 OE1 GLU 285
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    ATOM
            983 OE2 GLU 285
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    ATOM
                              21.898 12.082 23.823 1.00 33.23
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           984 C GLU 285
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            986 N GLN 286
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    ATOM
                               20.194 13.346 22.614 1.00 28.07
    ATOM
            987 CA GLN 286
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    ATOM
                                20.783 14.322 18.293 1.00 41.05
    ATOM
            991 OEI GLN 286
    ATOM
            992 NE2 GLN 286
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            993 C GLN 286
                               18.955 12.642 23.162 1.00 28.07
    ATOM
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     ATOM
            994 O GLN 286
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            995 N LEU 287
                              18.663 11.447 22.658 1.00 30.11
     ATOM
                               17.492 10.705 23.116 1.00 30.11
            996 CA LEU 287
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                               17.232 9.489 22.219 1.00 21.70
     ATOM 997 CB LEU 287
                               15.859 8.821 22.357 1.00 21.70
     ATOM 998 CG LEU 287
     ATOM 999 CD1 LEU 287
                                14.748 9.818 22.061 1.00 21.70
45
                                15.763 7.628 21.421 1.00 21.70
     ATOM 1000 CD2 LEU 287
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     ATOM 1001 C LEU 287
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     ATOM 1004 CA LYS 288
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    ATOM 1006 CG LYS 288
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    ATOM 1007 CD LYS 288
                               22.615 7.379 29.250 1.00 43.14
    ATOM 1008 CE LYS 288
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    ATOM 1009 NZ LYS 288
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    ATOM 1010 C LYS 288
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    ATOM 1011 O LYS 288
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    ATOM 1013 CA ASN 289
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    ATOM 1014 CB ASN 289
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    ATOM 1015 CG ASN 289
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    ATOM 1016 OD1 ASN 289
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    ATOM 1017 ND2 ASN 289
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    ATOM 1019 O ASN 289
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     ATOM 1026 C GLY 291
     ATOM 1027 O GLY 291
                              13.536 9.640 30.179 1.00 29.39
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     ATOM 1030 CB LEU 292
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     ATOM 1031 CG LEU 292
                               13.612 7.225 24.542 1.00 21.45
     ATOM 1032 CD1 LEU 292
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     ATOM 1033 CD2 LEU 292
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     ATOM 1037 CA GLY 293
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     ATOM 1038 C GLY 293
                               18.763 6.334 28.122 1.00 25.88
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     ATOM 1042 CB VAL 294
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     ATOM 1043 CG1 VAL 294
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     ATOM 1044 CG2 VAL 294
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     ATOM 1045 C VAL 294
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     ATOM 1046 O VAL 294
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     ATOM 1048 CA VAL 295
                                14.638 3.698 27.902 1.00 28.34
     ATOM 1049 CB VAL 295
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                                13.668 3.099 26.893 1.00 28.34
     ATOM 1050 CG1 VAL 295
                                14.159 3.431 29.317 1.00 28.34
     ATOM 1051 CG2 VAL 295
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    ATOM 1063 CG ASP 297
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    ATOM 1076 CG2 ILE 299
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    ATOM 1077 CG1 ILE 299
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    ATOM 1078 CD1 ILE 299
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    ATOM 1080 O ILE 299
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                               19.751 1.851 19.935 1.00 14.46
    ATOM 1082 CA PHE 300
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    ATOM 1083 CB PHE 300
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    ATOM 1084 CG PHE 300
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    ATOM 1085 CD1 PHE 300
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    ATOM 1086 CD2 PHE 300
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    ATOM 1087 CE1 PHE 300
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    ATOM 1088 CE2 PHE 300
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    ATOM 1089 CZ PHE 300
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    ATOM 1094 CB GLU 301
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    ATOM 1099 CB LEU 302
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    ATOM 1101 CD1 LEU 302
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    ATOM 1102 CD2 LEU 302
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                               18.027 -2.812 17.917 1.00 14.43
     ATOM 1103 C LEU 302
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    ATOM 1104 O LEU 302
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    ATOM 1112 CG LYS 304
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    ATOM 1113 CD LYS 304
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    ATOM 1114 CE LYS 304
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    ATOM 1115 NZ LYS 304
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    ATOM 1117 O LYS 304
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    ATOM 1119 CA SER 305
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                               20.610 -6.533 17.240 1.00 37.46
    ATOM 1120 CB SER 305
    ATOM 1121 OG SER 305
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    ATOM 1122 C SER 305
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    ATOM 1123 O SER 305
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    ATOM 1125 CA LEU 306
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    ATOM 1127 CG LEU 306
                                15.700 -5.190 15.432 1.00 15.99
                                14.504 -4.271 15.600 1.00 15.99
    ATOM 1128 CD1 LEU 306
                                15.244 -6.624 15.247 1.00 15.99
    ATOM 1129 CD2 LEU 306
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                               18.174 -5.330 12.439 1.00 25.47
    ATOM 1130 C LEU 306
    ATOM 1131 O LEU 306
                               17.596 -5.902 11.513 1.00 15.99
    ATOM 1132 N SER 307
                               19.182 -4.482 12.247 1.00 24.28
                               19.670 -4.160 10.907 1.00 24.28
    ATOM 1133 CA SER 307
                               20.910 -3.263 10.989 1.00 40.92
    ATOM 1134 CB SER 307
30
                                20.617 -2.028 11.622 1.00 40.92
    ATOM 1135 OG SER 307
    ATOM 1136 C SER 307
                               19.995 -5.422 10.107 1.00 24.28
                               19.625 -5.535 8.936 1.00 40.92
    ATOM 1137 O SER 307
                               20.644 -6.383 10.761 1.00 30.97
    ATOM 1138 N ALA 308
    ATOM 1139 CA ALA 308
                                21.027 -7.640 10.124 1.00 30.97
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                                22.004 -8.399 11.013 1.00 37.84
    ATOM 1140 CB ALA 308
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    ATOM 1141 C ALA 308
                               19.897 -9.336 8.853 1.00 37.84
    ATOM 1142 O ALA 308
                               18.737 -8.372 10.520 1.00 22.78
     ATOM 1143 N PHE 309
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     ATOM 1144 CA PHE 309
                                17.533 -9.166 10.292 1.00 22.78
     ATOM 1145 CB PHE 309
                                16.571 -9.037 11.477 1.00 30.14
                                17.032 -9.751 12.716 1.00 30.14
     ATOM 1146 CG PHE 309
                                16.299 -10.809 13.236 1.00 30.14
     ATOM 1147 CD1 PHE 309
                                 18.204 -9.372 13.359 1.00 30.14
     ATOM 1148 CD2 PHE 309
                                16.725 -11.481 14.378 1.00 30.14
     ATOM 1149 CE1 PHE 309
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                                18.640 -10.038 14.503 1.00 30.14
     ATOM 1150 CE2 PHE 309
                                17.896 -11.094 15.013 1.00 30.14
     ATOM 1151 CZ PHE 309
                               16.818 -8.813 8.990 1.00 22.78
     ATOM 1152 C PHE 309
                               16.068 -9.631 8.451 1.00 30.14
     ATOM 1153 O PHE 309
     ATOM 1154 N ASN 310
                               17.051 -7.598 8.496 1.00 35.30
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     ATOM 1156 CB ASN 310
                                17.109 -7.760 6.037 1.00 28.28
                               14.929 -7.339 7.229 1.00 35.30
     ATOM 1157 C ASN 310
     ATOM 1158 O ASN 310
                               14.395 -7.970 6.312 1.00 28.28
                               14.249 -6.831 8.251 1.00 27.52
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     ATOM 1160 CA LEU 311
                               12.803 -6.979 8.369 1.00 27.52
     ATOM 1161 CB LEU 311
                                12.351 -6.630 9.788 1.00 22.62
    ATOM 1162 CG LEU 311
                                12.950 -7.396 10.968 1.00 22.62
                                12.360 -6.864 12.268 1.00 22.62
    ATOM 1163 CD1 LEU 311
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    ATOM 1164 CD2 LEU 311
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    ATOM 1166 O LEU 311
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                               10.095 -5.789 5.968 1.00 16.74
    ATOM 1169 CB ASP 312
                                9.803 -6.578 4.673 1.00 16.35
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    ATOM 1170 CG ASP 312
                                8.924 -7.814 4.888 1.00 16.35
                                 8.591 -8.168 6.037 1.00 16.35
    ATOM 1171 OD1 ASP 312
                                 8.559 -8.446 3.876 1.00 16.35
     ATOM 1172 OD2 ASP 312
    ATOM 1173 C ASP 312
                               8.808 -5.354 6.678 1.00 16.74
    ATOM 1174 O ASP 312
                               8.535 -5.798 7.797 1.00 16.35
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                               8.007 -4.520 6.019 1.00 5.43
     ATOM 1175 N ASP 313
    ATOM 1176 CA ASP 313
                                6.758 -4.016 6.592 1.00 5.43
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                                5.974 -3.201 5.559 1.00 31.80
     ATOM 1178 CG ASP 313
                                6.670 -1.906 5.183 1.00 31.80
    ATOM 1179 OD1 ASP 313
                                 7.392 -1.340 6.033 1.00 31.80
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                                 6.493 -1.452 4.032 1.00 31.80
    ATOM 1180 OD2 ASP 313
    ATOM 1181 C ASP 313
                               5.849 -5.081 7.189 1.00 5.43
                               5.216 -4.849 8.221 1.00 31.80
     ATOM 1182 O ASP 313
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                               5.777 -6.238 6.543 1.00 12.98
                                4.934 -7.327 7.022 1.00 12.98
    ATOM 1184 CA THR 314
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                                4.825 -8.441 5.968 1.00 18.90
     ATOM 1185 CB THR 314
                                 4.249 -7.904 4.769 1.00 18.90
    ATOM 1186 OG1 THR 314
    ATOM 1187 CG2 THR 314
                                 3.960 -9.578 6.477 1.00 18.90
                               5.426 -7.910 8.349 1.00 12.98
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                               4.636 -8.124 9.268 1.00 18.90
     ATOM 1189 O THR 314
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    ATOM 1190 N GLU 315
                                6.731 -8.135 8.457 1.00 9.13
                                7.316 -8.685 9.675 1.00 9.13
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                                8.771 -9.078 9.427 1.00 11.49
     ATOM 1192 CB GLU 315
     ATOM 1193 CG GLU 315
                                8.870 -10.323 8.562 1.00 11.49
                                10.233 -10.544 7.945 1.00 11.49
     ATOM 1194 CD GLU 315
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                                10.964 -9.561 7.705 1.00 11.49
     ATOM 1195 OE1 GLU 315
                                10.558 -11.715 7.669 1.00 11.49
     ATOM 1196 OE2 GLU 315
                                7.180 -7.720 10.847 1.00 9.13
     ATOM 1197 C GLU 315
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     ATOM 1198 O GLU 315
     ATOM 1199 N VAL 316
                                7.376 -6.433 10.575 1.00 9.46
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     ATOM 1200 CA VAL 316
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                                7.655 -4.015 11.063 1.00 7.95
     ATOM 1201 CB VAL 316
     ATOM 1202 CG1 VAL 316
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     ATOM 1204 C VAL 316
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    ATOM 1207 CA ALA 317
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    ATOM 1209 C ALA 317
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    ATOM 1212 CA LEU 318
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    ATOM 1214 CG LEU 318
                                2.770 -10.494 10.514 1.00 10.49
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                                 1.297 -10.741 10.799 1.00 10.49
    ATOM 1216 CD2 LEU 318
    ATOM 1217 C LEU 318
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                                5.560 -8.325 15.366 1.00 9.43
    ATOM 1220 CA LEU 319
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    ATOM 1222 CG LEU 319
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                                 7.889 -8.977 17.182 1.00 24.05
    ATOM 1223 CD1 LEU 319
    ATOM 1224 CD2 LEU 319
                                 9.310 -7.356 15.922 1.00 24.05
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    ATOM 1225 C LEU 319
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                               4.287 -6.282 15.699 1.00 8.67
                                3.467 -5.325 16.437 1.00 8.67
    ATOM 1228 CA GLN 320
                                3.151 -4.102 15.573 1.00 10.94
    ATOM 1229 CB GLN 320
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    ATOM 1230 CG GLN 320
                                4.361 -3.256 15.218 1.00 10.94
    ATOM 1231 CD GLN 320
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    ATOM 1232 OE1 GLN 320
                                 4.889 -1.217 14.082 1.00 10.94
                                 2.773 -1.940 13.924 1.00 10.94
    ATOM 1233 NE2 GLN 320
                               2.169 -5.984 16.895 1.00 8.67
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    ATOM 1234 C GLN 320
    ATOM 1235 O GLN 320
                               1.708 -5.751 18.013 1.00 10.94
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    ATOM 1237 CA ALA 321
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     ATOM 1238 CB ALA 321
                                -0.136 -8.283 15.129 1.00 12.83
    ATOM 1239 C ALA 321
                               0.558 -8.460 17.523 1.00 9.21
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     ATOM 1241 N VAL 322
     ATOM 1242 CA VAL 322
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                                 3.783 -11.614 19.575 1.00 15.92
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    ATOM 1244 CG1 VAL 322
     ATOM 1245 CG2 VAL 322
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     ATOM 1246 C VAL 322
                               2.192 -9.256 19.960 1.00 9.10
     ATOM 1247 O VAL 322
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                               2.856 -8.106 19.893 1.00 11.07
     ATOM 1249 CA LEU 323
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     ATOM 1252 CD1 LEU 323
                                 6.039 -5.149 19.669 1.00 16.31
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     ATOM 1254 C LEU 323
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     ATOM 1260 CD1 LEU 324
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    ATOM 1267 CG MET 325
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     ATOM 1268 SD MET 325
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                                -6.284 -9.475 20.353 1.00 22.90
    ATOM 1269 CE MET 325
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     ATOM 1270 C MET 325
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     ATOM 1271 O MET 325
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    ATOM 1274 CB SER 326
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    ATOM 1275 OG SER 326
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    ATOM 1279 CA THR 327
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     ATOM 1281 OG1 THR 327
     ATOM 1282 CG2 THR 327
                                -3.716 -13.055 26.890 1.00 36.96
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     ATOM 1286 CA ASP 328
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     ATOM 1287 CB ASP 328
     ATOM 1288 CG ASP 328
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    ATOM 1289 OD1 ASP 328
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     ATOM 1290 OD2 ASP 328
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     ATOM 1295 CB ARG 329
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     ATOM 1296 CG ARG 329
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     ATOM 1297 CD ARG 329
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     ATOM 1298 NE ARG 329
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    ATOM 1299 CZ ARG 329
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                                 1.713 -6.552 28.290 1.00 38.88
     ATOM 1300 NH1 ARG 329
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     ATOM 1301 NH2 ARG 329
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     ATOM 1302 C ARG 329
     ATOM 1303 O ARG 329
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-3.999 -7.025 34.607 1.00 42.07
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    ATOM 1306 CB SER 330
    ATOM 1307 C SER 330
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    ATOM 1309 N GLY 331
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    ATOM 1310 CA GLY 331
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    ATOM 1312 O GLY 331
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    ATOM 1316 CG LEU 332
     ATOM 1317 CD1 LEU 332
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    ATOM 1318 CD2 LEU 332
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    ATOM 1319 C LEU 332
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     ATOM 1324 CG LEU 333
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     ATOM 1327 C LEU 333
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     ATOM 1328 O LEU 333
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    ATOM 1329 N CYS 334
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     ATOM 1330 CA CYS 334
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     ATOM 1331 CB CYS 334
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     ATOM 1333 C CYS 334
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     ATOM 1337 CB VAL 335
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     ATOM 1338 CG1 VAL 335
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     ATOM 1339 CG2 VAL 335
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     ATOM 1341 O VAL 335
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     ATOM 1343 CA ASP 336
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     ATOM 1344 CB ASP 336
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     ATOM 1345 CG ASP 336
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     ATOM 1346 OD1 ASP 336
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     ATOM 1347 OD2 ASP 336
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     ATOM 1348 C ASP 336
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     ATOM 1349 O ASP 336
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     ATOM 1351 CA LYS 337
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     ATOM 1353 C LYS 337
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     ATOM 1354 O LYS 337
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	ATOM	1356 CA ILE 338	-6.879 -12.376 23.078 1.00 24.65
	ATOM	1357 CB ILE 338	-6.543 -11.380 24.215 1.00 20.45
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5	ATOM	1359 CG1 ILE 338	-7.632 -10.308 24.308 1.00 20.45
	ATOM	1360 CD1 ILE 338	-7.479 -9.374 25.486 1.00 20.45
	ATOM		-5.744 -13.388 22.911 1.00 24.65
	ATOM	1362 O ILE 338	-4.948 -13.288 21.974 1.00 20.45
	ATOM	1363 N GLU 339	-5.700 -14.383 23.795 1.00 35.34
10	ATOM	1364 CA GLU 339	-4.673 -15.422 23.745 1.00 35.34
	ATOM	1365 CB GLU 339	-4.836 -16.388 24.916 1.00 29.51
	ATOM	1366 C GLU 339	-4.744 -16.180 22.421 1.00 35.34
	ATOM	1367 O GLU 339	-3.720 -16.421 21.777 1.00 29.51
	ATOM	1368 N LYS 340	-5.959 -16.536 22.009 1.00 24.19
15	ATOM	1369 CA LYS 340	-6.168 -17.256 20.755 1.00 24.19
	ATOM	1370 CB LYS 340	-7.627 -17.671 20.624 1.00 23.97
	ATOM	1371 C LYS 340	-5.754 -16.377 19.576 1.00 24.19
	ATOM	1372 O LYS 340	-5.197 -16.860 18.586 1.00 23.97
	ATOM	1373 N SER 341	-6.000 -15.079 19.708 1.00 16.85
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	ATOM	1375 CB SER 341	-6.223 -12.744 19.033 1.00 26.59
	ATOM	1376 OG SER 341	-5.852 -11.765 18.080 1.00 26.59
	ATOM	1377 C SER 341	-4.137 -14.026 18.500 1.00 16.85
	ATOM	1378 O SER 341	-3.638 -14.042 17.374 1.00 26.59
25	ATOM	1379 N GLN 342	-3.406 -13.932 19.608 1.00 17.35
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ATOM 1560 CB PHE 363 ATOM 1561 CG PHE 363 ATOM 1562 CD1 PHE 363 ATOM 1563 CD2 PHE 363 ATOM 1563 CD2 PHE 363 ATOM 1564 CEI PHE 363 ATOM 1565 CE2 PHE 363 ATOM 1565 CE2 PHE 363 ATOM 1566 CZ PHE 363 ATOM 1566 CZ PHE 363 ATOM 1566 CZ PHE 363 ATOM 1567 C PHE 363 ATOM 1568 O PHE 363 ATOM 1568 O PHE 363 ATOM 1569 N TRP 364 ATOM 1570 CA TRP 364 ATOM 1570 CA TRP 364 ATOM 1571 CB TRP 364 ATOM 1572 CG TRP 364 ATOM 1575 CG TRP 364 ATOM 1575 CG TRP 364 ATOM 1576 CD1 TRP 364 ATOM 1576 CD1 TRP 364 ATOM 1578 CZ2 TRP 364 ATOM 1579 CZ3 TRP 364 ATOM 1579 CZ3 TRP 364 ATOM 1579 CZ3 TRP 364 ATOM 1578 CZ2 TRP 364 ATOM 1579 CZ3 TRP 364 ATOM 1581 C TRP 364 ATOM 1582 O TRP 364 ATOM 1588 C PRO 365 ATOM 1585 CA PRO 365 ATOM 1586 CB PRO 365 ATOM 1587 CG PRO 365 ATOM 1587 CG PRO 365 ATOM 1588 C PRO 365 ATOM 1589 O PRO 365 ATOM 1590 N LYS 366 ATOM 1590 CLYS 366 ATOM 1590 CLYS 366 ATOM 1595 CE LYS 366 ATOM 1595 CE LYS 366 ATOM 1595 C LYS 366 ATOM 1595 C LYS 366 ATOM 1595 C LYS 366 ATOM 1596 NZ LYS 366 ATOM 1597 C LYS 366 ATOM 1598 O LYS 366 ATOM 1597 C LYS 366 ATOM 1598 O LYS 366 ATOM 1599 N LEU 367 ATOM 1600 CA LEU 367 ATOM 1600 CA LEU 367 ATOM 1600 CA LEU 367		ATOM	1558 N PHE 363	
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ATOM 1562 CD1 PHE 363 ATOM 1563 CD2 PHE 363 ATOM 1564 CE1 PHE 363 ATOM 1565 CE2 PHE 363 ATOM 1565 CE2 PHE 363 ATOM 1566 CZ PHE 363 ATOM 1566 CZ PHE 363 ATOM 1566 CZ PHE 363 ATOM 1566 CZ PHE 363 ATOM 1566 CZ PHE 363 ATOM 1568 O PHE 363 ATOM 1569 N TRP 364 ATOM 1570 CA TRP 364 ATOM 1570 CA TRP 364 ATOM 1571 CB TRP 364 ATOM 1572 CG TRP 364 ATOM 1573 CD2 TRP 364 ATOM 1575 CE3 TRP 364 ATOM 1575 CE3 TRP 364 ATOM 1576 CD1 TRP 364 ATOM 1576 CD1 TRP 364 ATOM 1576 CD1 TRP 364 ATOM 1578 CZ2 TRP 364 ATOM 1580 CH2		ATOM	1560 CB PHE 363	
ATOM 1563 CD2 PHE 363		ATOM	1561 CG PHE 363	
10 ATOM 1564 CE1 PHE 363 ATOM 1565 CE2 PHE 363 ATOM 1566 CZ PHE 363 ATOM 1566 CZ PHE 363 ATOM 1567 C PHE 363 ATOM 1568 O PHE 363 ATOM 1568 O PHE 363 ATOM 1569 N TRP 364 ATOM 1570 CA TRP 364 ATOM 1571 CB TRP 364 ATOM 1573 CD2 TRP 364 ATOM 1573 CD2 TRP 364 ATOM 1575 CE3 TRP 364 ATOM 1576 CD1 TRP 364 ATOM 1577 CE2 TRP 364 ATOM 1577 CE3 TRP 364 ATOM 1578 CZ2 TRP 364 ATOM 1578 CZ2 TRP 364 ATOM 1578 CZ2 TRP 364 ATOM 1579 CZ3 TRP 364 ATOM 1580 CH2 TRP 364 ATOM 1590 N LYS 366 ATOM 1590 N LYS 366 ATOM 1590 CLYS 366 ATOM 1590 CLYS 366 ATOM 1590 N LYS 366 ATOM 1590 N		ATOM		
ATOM 1565 CE2 PHE 363 ATOM 1566 CZ PHE 363 ATOM 1567 C PHE 363 ATOM 1568 O PHE 363 ATOM 1568 O PHE 363 ATOM 1568 N TRP 364 ATOM 1569 N TRP 364 ATOM 1570 CA TRP 364 ATOM 1571 CB TRP 364 ATOM 1572 CG TRP 364 ATOM 1573 CD2 TRP 364 ATOM 1575 CE3 TRP 364 ATOM 1575 CE3 TRP 364 ATOM 1576 CD1 TRP 364 ATOM 1577 NE1 TRP 364 ATOM 1578 CZ2 TRP 364 ATOM 1578 CZ2 TRP 364 ATOM 1578 CZ2 TRP 364 ATOM 1578 CZ2 TRP 364 ATOM 1580 CH2 TRP 364 ATOM 1590 N LYS 366 ATOM 1		ATOM		
ATOM 1566 CZ PHE 363	10	ATOM		
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ATOM 1582 O TRP 364 12.595 -16.133 16.087 1.00 17.81 ATOM 1583 N PRO 365 13.779 -18.051 16.137 1.00 18.31 30 ATOM 1584 CD PRO 365 14.342 -19.314 15.625 1.00 25.61 ATOM 1585 CA PRO 365 14.038 -17.920 17.577 1.00 18.31 ATOM 1586 CB PRO 365 14.939 -19.118 17.874 1.00 25.61 ATOM 1587 CG PRO 365 14.500 -20.130 16.882 1.00 25.61 ATOM 1588 C PRO 365 14.387 -15.963 18.926 1.00 25.61 ATOM 1590 N LYS 366 15.699 -16.207 17.112 1.00 25.16 ATOM 1591 CA LYS 366 16.439 -14.968 17.338 1.00 25.16 ATOM 1592 CB LYS 366 16.439 -14.968 17.338 1.00 25.16 ATOM 1593 CG LYS 366 18.679 -15.792 16.417 1.00 40.51 ATOM 1595 CE LYS 366 19.664 -15.607 15.278 1.00 40.51 ATOM 1596 NZ LYS 366 20.884 -16.492 15.440 1.00 40.51 ATOM 1597 C LYS 366 15.593 -12.893 18.202 1.00 40.51 ATOM 1598 O LYS 366 15.593 -12.893 18.202 1.00 40.51 ATOM 1599 N LEU 367 14.661 -13.666 16.307 1.00 25.30 ATOM 1600 CA LEU 367 12.989 -12.520 14.845 1.00 27.80				
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ATOM 1586 CB PRO 365 14.939 -19.118 17.874 1.00 25.61 ATOM 1587 CG PRO 365 14.500 -20.130 16.882 1.00 25.61 ATOM 1588 C PRO 365 14.732 -16.606 17.933 1.00 18.31 35 ATOM 1589 O PRO 365 14.387 -15.963 18.926 1.00 25.61 ATOM 1590 N LYS 366 15.699 -16.207 17.112 1.00 25.16 ATOM 1591 CA LYS 366 16.439 -14.968 17.338 1.00 25.16 ATOM 1592 CB LYS 366 17.537 -14.805 16.289 1.00 40.51 ATOM 1593 CG LYS 366 18.679 -15.792 16.417 1.00 40.51 ATOM 1594 CD LYS 366 19.664 -15.607 15.278 1.00 40.51 ATOM 1595 CE LYS 366 20.884 -16.492 15.440 1.00 40.51 ATOM 1596 NZ LYS 366 21.800 -16.360 14.275 1.00 40.51 ATOM 1598 O LYS 366 15.593 -12.893 18.202 1.00 40.51 ATOM 1599 N LEU 367 14.661 -13.666 16.307 1.00 25.30 ATOM 1600 CA LEU 367 13.729 -12.551 16.184 1.00 25.30 ATOM 1601 CB LEU 367 12.989 -12.620 14.845 1.00 27.80	50			
ATOM 1587 CG PRO 365 14.500 -20.130 16.882 1.00 25.61 ATOM 1588 C PRO 365 14.732 -16.606 17.933 1.00 18.31 35 ATOM 1589 O PRO 365 14.387 -15.963 18.926 1.00 25.61 ATOM 1590 N LYS 366 15.699 -16.207 17.112 1.00 25.16 ATOM 1591 CA LYS 366 16.439 -14.968 17.338 1.00 25.16 ATOM 1592 CB LYS 366 17.537 -14.805 16.289 1.00 40.51 ATOM 1593 CG LYS 366 18.679 -15.792 16.417 1.00 40.51 ATOM 1594 CD LYS 366 19.664 -15.607 15.278 1.00 40.51 ATOM 1595 CE LYS 366 20.884 -16.492 15.440 1.00 40.51 ATOM 1596 NZ LYS 366 21.800 -16.360 14.275 1.00 40.51 ATOM 1598 O LYS 366 15.521 -13.747 17.317 1.00 25.16 ATOM 1599 N LEU 367 14.661 -13.666 16.307 1.00 25.30 ATOM 1600 CA LEU 367 13.729 -12.551 16.184 1.00 25.30 ATOM 1601 CB LEU 367 12.989 -12.620 14.845 1.00 27.80				
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35 ATOM 1589 O PRO 365 14.387 - 15.963 18.926 1.00 25.61 ATOM 1590 N LYS 366 15.699 - 16.207 17.112 1.00 25.16 ATOM 1591 CA LYS 366 16.439 - 14.968 17.338 1.00 25.16 ATOM 1592 CB LYS 366 17.537 - 14.805 16.289 1.00 40.51 ATOM 1593 CG LYS 366 18.679 - 15.792 16.417 1.00 40.51 ATOM 1594 CD LYS 366 19.664 - 15.607 15.278 1.00 40.51 ATOM 1595 CE LYS 366 20.884 - 16.492 15.440 1.00 40.51 ATOM 1596 NZ LYS 366 21.800 - 16.360 14.275 1.00 40.51 ATOM 1597 C LYS 366 15.521 - 13.747 17.317 1.00 25.16 ATOM 1599 N LEU 367 14.661 - 13.666 16.307 1.00 25.30 ATOM 1600 CA LEU				14.732 -16.606 17.933 1.00 18.31
ATOM 1590 N LYS 366 15.699 -16.207 17.112 1.00 25.16 ATOM 1591 CA LYS 366 16.439 -14.968 17.338 1.00 25.16 ATOM 1592 CB LYS 366 17.537 -14.805 16.289 1.00 40.51 ATOM 1593 CG LYS 366 18.679 -15.792 16.417 1.00 40.51 ATOM 1594 CD LYS 366 19.664 -15.607 15.278 1.00 40.51 ATOM 1595 CE LYS 366 20.884 -16.492 15.440 1.00 40.51 ATOM 1596 NZ LYS 366 21.800 -16.360 14.275 1.00 40.51 ATOM 1597 C LYS 366 15.521 -13.747 17.317 1.00 25.16 ATOM 1598 O LYS 366 15.593 -12.893 18.202 1.00 40.51 ATOM 1599 N LEU 367 14.661 -13.666 16.307 1.00 25.30 ATOM 1600 CA LEU 367 13.729 -12.551 16.184 1.00 25.30 ATOM 1601 CB LEU 367 12.989 -12.620 14.845 1.00 27.80	35			
ATOM 1591 CA LYS 366 16.439 -14.968 17.338 1.00 25.16 ATOM 1592 CB LYS 366 17.537 -14.805 16.289 1.00 40.51 ATOM 1593 CG LYS 366 18.679 -15.792 16.417 1.00 40.51 ATOM 1594 CD LYS 366 19.664 -15.607 15.278 1.00 40.51 ATOM 1595 CE LYS 366 20.884 -16.492 15.440 1.00 40.51 ATOM 1596 NZ LYS 366 21.800 -16.360 14.275 1.00 40.51 ATOM 1597 C LYS 366 15.521 -13.747 17.317 1.00 25.16 ATOM 1598 O LYS 366 15.593 -12.893 18.202 1.00 40.51 ATOM 1599 N LEU 367 14.661 -13.666 16.307 1.00 25.30 ATOM 1600 CA LEU 367 13.729 -12.551 16.184 1.00 25.30 ATOM 1601 CB LEU 367 12.989 -12.620 14.845 1.00 27.80				15.699 -16.207 17.112 1.00 25.16
ATOM 1592 CB LYS 366 17.537 -14.805 16.289 1.00 40.51 ATOM 1593 CG LYS 366 18.679 -15.792 16.417 1.00 40.51 40 ATOM 1594 CD LYS 366 19.664 -15.607 15.278 1.00 40.51 ATOM 1595 CE LYS 366 20.884 -16.492 15.440 1.00 40.51 ATOM 1596 NZ LYS 366 21.800 -16.360 14.275 1.00 40.51 ATOM 1597 C LYS 366 15.521 -13.747 17.317 1.00 25.16 ATOM 1598 O LYS 366 15.593 -12.893 18.202 1.00 40.51 ATOM 1599 N LEU 367 14.661 -13.666 16.307 1.00 25.30 ATOM 1600 CA LEU 367 13.729 -12.551 16.184 1.00 25.30 ATOM 1601 CB LEU 367 12.989 -12.620 14.845 1.00 27.80		ATOM		16.439 -14.968 17.338 1.00 25.16
40 ATOM 1594 CD LYS 366 19.664 -15.607 15.278 1.00 40.51 ATOM 1595 CE LYS 366 20.884 -16.492 15.440 1.00 40.51 ATOM 1596 NZ LYS 366 21.800 -16.360 14.275 1.00 40.51 ATOM 1597 C LYS 366 15.521 -13.747 17.317 1.00 25.16 ATOM 1598 O LYS 366 15.593 -12.893 18.202 1.00 40.51 45 ATOM 1599 N LEU 367 14.661 -13.666 16.307 1.00 25.30 ATOM 1600 CA LEU 367 13.729 -12.551 16.184 1.00 25.30 ATOM 1601 CB LEU 367 12.989 -12.620 14.845 1.00 27.80				17.537 -14.805 16.289 1.00 40.51
ATOM 1595 CE LYS 366 20.884 -16.492 15.440 1.00 40.51 ATOM 1596 NZ LYS 366 21.800 -16.360 14.275 1.00 40.51 ATOM 1597 C LYS 366 15.521 -13.747 17.317 1.00 25.16 ATOM 1598 O LYS 366 15.593 -12.893 18.202 1.00 40.51 ATOM 1599 N LEU 367 14.661 -13.666 16.307 1.00 25.30 ATOM 1600 CA LEU 367 13.729 -12.551 16.184 1.00 25.30 ATOM 1601 CB LEU 367 12.989 -12.620 14.845 1.00 27.80		ATOM	1593 CG LYS 366	18.679 -15.792 16.417 1.00 40.51
ATOM 1596 NZ LYS 366 21.800 -16.360 14.275 1.00 40.51 ATOM 1597 C LYS 366 15.521 -13.747 17.317 1.00 25.16 ATOM 1598 O LYS 366 15.593 -12.893 18.202 1.00 40.51 ATOM 1599 N LEU 367 14.661 -13.666 16.307 1.00 25.30 ATOM 1600 CA LEU 367 13.729 -12.551 16.184 1.00 25.30 ATOM 1601 CB LEU 367 12.989 -12.620 14.845 1.00 27.80	40	ATOM	1594 CD LYS 366	
ATOM 1597 C LYS 366 15.521 -13.747 17.317 1.00 25.16 ATOM 1598 O LYS 366 15.593 -12.893 18.202 1.00 40.51 45 ATOM 1599 N LEU 367 14.661 -13.666 16.307 1.00 25.30 ATOM 1600 CA LEU 367 13.729 -12.551 16.184 1.00 25.30 ATOM 1601 CB LEU 367 12.989 -12.620 14.845 1.00 27.80		ATOM	1595 CE LYS 366	20.884 -16.492 15.440 1.00 40.51
ATOM 1598 O LYS 366 15.593 -12.893 18.202 1.00 40.51 45 ATOM 1599 N LEU 367 14.661 -13.666 16.307 1.00 25.30 ATOM 1600 CA LEU 367 13.729 -12.551 16.184 1.00 25.30 ATOM 1601 CB LEU 367 12.989 -12.620 14.845 1.00 27.80		ATOM	1596 NZ LYS 366	21.800 -16.360 14.275 1.00 40.51
45 ATOM 1599 N LEU 367 14.661 -13.666 16.307 1.00 25.30 ATOM 1600 CA LEU 367 13.729 -12.551 16.184 1.00 25.30 ATOM 1601 CB LEU 367 12.989 -12.620 14.845 1.00 27.80		ATOM	1597 C LYS 366	
ATOM 1600 CA LEU 367 13.729 -12.551 16.184 1.00 25.30 ATOM 1601 CB LEU 367 12.989 -12.620 14.845 1.00 27.80		ATOM	1598 O LYS 366	
ATOM 1601 CB LEU 367 12.989 -12.620 14.845 1.00 27.80	45	ATOM	1599 N LEU 367	
		ATOM	1600 CA LEU 367	
ATOM 1602 CG LEU 367 11.964-11.519 14.561 1.00 27.80				
		ATOM		
				12.621 -10.147 14.679 1.00 27.80
50 ATOM 1604 CD2 LEU 367 11.367 -11.724 13.175 1.00 27.8	50	ATOM	1604 CD2 LEU 367	11.367 -11.724 13.175 1.00 27.80

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ATOM 1605 C LEU 367
                               12.730 -12.596 17.332 1.00 25.30
    ATOM 1606 O LEU 367
                               12.337 -11.563 17.877 1.00 27.80
    ATOM 1607 N LEU 368
                               12.345 -13.807 17.712 1.00 26.12
    ATOM 1608 CA LEU 368
                                11.396 -14.019 18.793 1.00 26.12
                                11.105 -15.515 18.919 1.00 33.27
    ATOM 1609 CB LEU 368
                                9.696 -15.976 19.289 1.00 33.27
    ATOM 1610 CG LEU 368
    ATOM 1611 CD1 LEU 368
                                 8.640 -15.182 18.529 1.00 33.27
    ATOM 1612 CD2 LEU 368
                                 9.582 -17.460 18.976 1.00 33.27
    ATOM 1613 C LEU 368
                               11.973 -13.466 20.096 1.00 26.12
                               11,249 -12,920 20,930 1.00 33.27
    ATOM 1614 O LEU 368
10
                               13.289 -13.571 20.244 1.00 24.39
    ATOM 1615 N MET 369
                                13.971 -13.076 21.432 1.00 24.39
    ATOM 1616 CA MET 369
     ATOM 1617 CB MET 369
                                15.382 -13.656 21.511 1.00 47.44
    ATOM 1618 CG MET 369
                                15.407 -15.096 22.009 1.00 47.44
                                16.850 -16.029 21.464 1.00 47.44
    ATOM 1619 SD MET 369
15
                                18.186 -15.114 22.246 1.00 47.44
     ATOM 1620 CE MET 369
                                13.996 -11.552 21.491 1.00 24.39
     ATOM 1621 C MET 369
     ATOM 1622 O MET 369
                               14.212 -10.971 22.557 1.00 47.44
                               13.749 -10.904 20.354 1.00 27.31
     ATOM 1623 N LYS 370
     ATOM 1624 CA LYS 370
                                13.713 -9.445 20.297 1.00 27.31
20
                                13.739 -8.951 18.847 1.00 28.20
     ATOM 1625 CB LYS 370
                                15.004 -9:312 18.090 1.00 28.20
     ATOM 1626 CG LYS 370
                                16.231 -8.810 18.824 1.00 28.20
     ATOM 1627 CD LYS 370
     ATOM 1628 CE LYS 370
                                17.512 -9.244 18.142 1.00 28.20
                                18.696 -8.851 18.952 1.00 28.20
     ATOM 1629 NZ LYS 370
25
                               12.453 -8.945 21.002 1.00 27.31
     ATOM 1630 C LYS 370
     ATOM 1631 O LYS 370
                               12.424 -7.835 21.535 1.00 28.20
     ATOM 1632 N VAL 371
                                11.413 -9.776 21.009 1.00 26.41
                                10.157 -9.432 21.668 1.00 26.41
     ATOM 1633 CA VAL 371
                                 9.109 -10.561 21.512 1.00 25.61
     ATOM 1634 CB VAL 371
30
                                 7.825 -10.205 22.245 1.00 25.61
     ATOM 1635 CG1 VAL 371
     ATOM 1636 CG2 VAL 371
                                 8.819 -10.805 20.044 1.00 25.61
                                10.450 -9.205 23.151 1.00 26.41
     ATOM 1637 C VAL 371
     ATOM 1638 O VAL 371
                                9.962 -8.248 23.752 1.00 25.61
                                11.294 -10.065 23.713 1.00 26.28
     ATOM 1639 N THR 372
35
                                11.683 -9.972 25.116 1.00 26.28
     ATOM 1640 CA THR 372
                                12.656 -11.109 25.500 1.00 28.14
     ATOM 1641 CB THR 372
                                 12.025 -12.377 25.275 1.00 28.14
     ATOM 1642 OG1 THR 372
                                 13.055 -11.001 26.965 1.00 28.14
     ATOM 1643 CG2 THR 372
                               12.358 -8.624 25.372 1.00 26.28
     ATOM 1644 C THR 372
40
     ATOM 1645 O THR 372
                                12.047 -7.937 26.350 1.00 28.14
                               13.269 -8.247 24.478 1.00 15.09
     ATOM 1646 N ASP 373
                                13.977 -6.979 24.588 1.00 15.09
     ATOM 1647 CA ASP 373
     ATOM 1648 CB ASP 373
                                14.976 -6.822 23.435 1.00 37.94
     ATOM 1649 CG ASP 373
                                16.065 -7.893 23.445 1.00 37.94
45
                                 16.248 -8.571 24.483 1.00 37.94
     ATOM 1650 OD1 ASP 373
                                 16.750 -8.052 22.410 1.00 37.94
     ATOM 1651 OD2 ASP 373
                               12.969 -5.833 24.577 1.00 15.09
     ATOM 1652 C ASP 373
     ATOM 1653 O ASP 373
                               13.040 -4.928 25.407 1.00 37.94
                               12.008 -5.901 23.659 1.00 17.04
     ATOM 1654 N LEU 374
50
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	ATOM	1655 CA LEU 374	10.974 -4.880 23.549 1.00 17.04
	ATOM	1656 CB LEU 374	10.071 -5.155 22.344 1.00 20.58
	ATOM	1657 CG LEU 374	10.624 -4.720 20.985 1.00 20.58
	ATOM	1658 CD1 LEU 374	9.826 -5.352 19.862 1.00 20.58
5	ATOM	1659 CD2 LEU 374	10.599 -3.202 20.882 1.00 20.58
J	ATOM	1660 C LEU 374	10.145 -4.786 24.825 1.00 17.04
	ATOM	1661 O LEU 374	9.783 -3.688 25.256 1.00 20.58
	ATOM	1662 N ARG 375	9.850 -5.935 25.430 1.00 20.46
	ATOM	1663 CA ARG 375	9.080 -5.977 26.673 1.00 20.46
10	ATOM	1664 CB ARG 375	8.873 -7.422 27.140 1.00 55.89
10	ATOM	1665 CG ARG 375	8.180 -8.354 26.152 1.00 55.89
	ATOM	1666 CD ARG 375	6.692 -8.084 26.027 1.00 55.89
	ATOM	1667 NE ARG 375	5.943 -9.338 25.968 1.00 55.89
	ATOM	1668 CZ ARG 375	5.054 -9.654 25.028 1.00 55.89
15	ATOM	1669 NH1 ARG 375	•
13	ATOM	1670 NH2 ARG 375	
	ATOM	1671 C ARG 375	9.874 -5.221 27.735 1.00 20.46
	ATOM	1672 O ARG 375	9.328 -4.391 28.463 1.00 55.89
	ATOM	1673 N MET 376	11.174 -5.502 27.794 1.00 20.10
20	ATOM	1674 CA MET 376	12.076 -4.863 28.744 1.00 20.10
20	ATOM	1675 CB MET 376	13.493 -5.417 28.580 1.00 63.73
	ATOM	1676 CG MET 376	13.956 -6.310 29.722 1.00 63.73
	ATOM	1677 SD MET 376	14.494 -5.373 31.182 1.00 63.73
	ATOM	1678 CE MET 376	12.934 -5.151 32.087 1.00 63.73
25	ATOM	1679 C MET 376	12.081 -3.347 28.566 1.00 20.10
23	ATOM	1680 O MET 376	11.973 -2.602 29.539 1.00 63.73
	ATOM	1681 N ILE 377	12.194 -2.896 27.321 1.00 30.02
	ATOM	1682 CA ILE 377	12.198 -1.469 27.014 1.00 30.02
	ATOM	1683 CB ILE 377	12.329 -1.228 25.488 1.00 19.31
30	ATOM	1684 CG2 ILE 377	12.088 0.242 25.152 1.00 19.31
50	ATOM	1685 CG1 ILE 377	13.711 -1.685 25.011 1.00 19.31
	ATOM	1686 CD1 ILE 377	13.906 -1.634 23.507 1.00 19.31
	ATOM	1687 C ILE 377	10.915 -0.821 27.542 1.00 30.02
	ATOM	1688 O ILE 377	10.962 0.216 28.211 1.00 19.31
35	ATOM	1689 N GLY 378	9.779 -1.455 27.266 1.00 21.85
-	ATOM	1690 CA GLY 378	8.505 -0.936 27.729 1.00 21.85
	ATOM	1691 C GLY 378	8.459 -0.821 29.243 1.00 21.85
	ATOM	1692 O GLY 378	7.990 0.185 29.779 1.00 34.01
	ATOM	1693 N ALA 379	8.967 -1.842 29.928 1.00 31.30
40	ATOM	1694 CA ALA 379	8.996 -1.870 31.388 1.00 31.30
	ATOM	1695 CB ALA 379	9.471 -3.231 31.880 1.00 30.06
	ATOM	1696 C ALA 379	9.895 -0.763 31.938 1.00 31.30
	ATOM	1697 O ALA 379	9.482 0.002 32.810 1.00 30.06
	ATOM	1698 N CYS 380	11.117 -0.677 31.418 1.00 28.61
45	ATOM	1699 CA CYS 380	12.067 0.349 31.841 1.00 28.61
	ATOM	1700 CB CYS 380	13.360 0.268 31.025 1.00 60.26
	ATOM	1700 CB CYS 380	14.499 -1.067 31.470 1.00 60.26
	ATOM	1701 BG C16 360	11.449 1.730 31.658 1.00 28.61
	ATOM	1702 C CYS 380	11.516 2.573 32.554 1.00 60.26
50	ATOM	1704 N HIS 381	10.840 1.957 30.498 1.00 30.42
		1110	

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	ATOM	1705 CA HIS 381	10.212 3.243 30.216 1.00 30.42
	ATOM	1706 CB HIS 381	9.696 3.306 28.779 1.00 16.49
	ATOM	1707 CG HIS 381	8.942 4.562 28.472 1.00 16.49
	ATOM	1708 CD2 HIS 381	9.370 5.805 28.151 1.00 16.49
5	ATOM	1709 ND1 HIS 381	7.566 4.633 28.524 1.00 16.49
	ATOM	1710 CE1 HIS 381	7.180 5.866 28.251 1.00 16.49
	ATOM	1711 NE2 HIS 381	8.255 6.596 28.021 1.00 16.49
	ATOM	1712 C HIS 381	9.073 3.539 31.182 1.00 30.42
	ATOM	1713 O HIS 381	8.856 4.690 31.552 1.00 16.49
10	ATOM	1714 N ALA 382	8.330 2.506 31.564 1.00 22.89
	ATOM	1715 CA ALA 382	7.218 2.666 32.493 1.00 22.89
	ATOM	1716 CB ALA 382	6.520 1.336 32.708 1.00 34.50
	ATOM	1717 C ALA 382	7.738 3.213 33.819 1.00 22.89
	ATOM	1718 O ALA 382	7.219 4.200 34.343 1.00 34.50
15	ATOM	1719 N SER 383	8.789 2.586 34.336 1.00 26.39
	ATOM	1720 CA SER 383	9.400 3.006 35.591 1.00 26.39
	ATOM	1721 CB SER 383	10.510 2.030 35.985 1.00 52.94
	ATOM	1722 OG SER 383	10.015 0.702 36.046 1.00 52.94
	ATOM	1723 C SER 383	9.966 4.418 35.470 1.00 26.39
20	ATOM	1724 O SER 383	9.772 5.253 36.357 1.00 52.94
	ATOM	1725 N ARG 384	10.662 4.683 34.368 1.00 30.36
	ATOM	1726 CA ARG 384	11.249 5.995 34.134 1.00 30.36
	ATOM	1727 CB ARG 384	12.116 5.977 32.874 1.00 37.39 12.601 7.344 32.431 1.00 37.39
25	ATOM	1728 CG ARG 384	
25	ATOM	1729 CD ARG 384 1730 NE ARG 384	14.070 7.321 32.060 1.00 37.39 14.935 7.597 33.204 1.00 37.39
	ATOM		15.750 8.646 33.291 1.00 37.39
	ATOM ATOM	1731 CZ ARG 384 1732 NH1 ARG 384	15.730 8.640 33.291 1.00 37.39
	ATOM	1732 NH1 ARG 384	16.488 8.819 34.376 1.00 37.39
30	ATOM	1734 C ARG 384	10.169 7.067 34.030 1.00 30.36
50	ATOM	1735 O ARG 384	10.301 8.144 34.616 1.00 37.39
	ATOM	1736 N PHE 385	9.078 6.749 33.338 1.00 24.47
	ATOM	1737 CA PHE 385	7.980 7.693 33.171 1.00 24.47
	ATOM	1738 CB PHE 385	6.859 7.092 32.319 1.00 28.70
35	ATOM	1739 CG PHE 385	5.710 8.036 32.075 1.00 28.70
	ATOM	1740 CD1 PHE 385	5.795 9.017 31.092 1.00 28.70
	ATOM	1741 CD2 PHE 385	4.549 7.954 32.836 1.00 28.70
	ATOM	1742 CE1 PHE 385	4.740 9.903 30.874 1.00 28.70
	ATOM	1743 CE2 PHE 385	3.491 8.835 32.624 1.00 28.70
40	ATOM	1744 CZ PHE 385	3.587 9.812 31.641 1.00 28.70
	ATOM	1745 C PHE 385	7.436 8.097 34.533 1.00 24.47
	ATOM	1746 O PHE 385	7.250 9.285 34.805 1.00 28.70
	ATOM	1747 N LEU 386	7.208 7.107 35.391 1.00 31.13
	ATOM	1748 CA LEU 386	6.690 7.352 36.734 1.00 31.13
45	ATOM	1749 CB LEU 386	6.596 6.044 37.513 1.00 39.10
	ATOM	1750 C LEU 386	7.577 8.348 37.474 1.00 31.13
	ATOM	1751 O LEU 386	7.085 9.201 38.217 1.00 39.10
	ATOM	1752 N HIS 387	8.884 8.254 37.243 1.00 36.46
	ATOM	1753 CA HIS 387	9.837 9.152 37.881 1.00 36.46
50	ATOM	1754 CB HIS 387	11.258 8.589 37.794 1.00 62.78

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	ATOM ATOM ATOM	1755 CG HIS 387 1756 CD2 HIS 387 1757 ND1 HIS 387	11.459 7.338 38.590 1.00 62.78 10.601 6.614 39.346 1.00 62.78 12.675 6.689 38.663 1.00 62.78
	ATOM	1758 CE1 HIS 387	12.554 5.620 39.431 1.00 62.78
5	ATOM	1759 NE2 HIS 387	11.309 5.550 39.856 1.00 62.78
,	ATOM	1760 C HIS 387	9.778 10.544 37.266 1.00 36.46
	ATOM	1761 O HIS 387	9.885 11.543 37.979 1.00 62.78
	ATOM	1762 N MET 388	9.587 10.612 35.950 1.00 33.41
	ATOM	1763 CA MET 388	9.505 11.894 35.258 1.00 33.41
10	ATOM	1764 CB MET 388	9,269 11.703 33.755 1.00 42.63
	ATOM	1765 CG MET 388	10.456 11.144 32.982 1.00 42.63
	ATOM	1766 SD MET 388	10.253 11.325 31.192 1.00 42.63
	ATOM	1767 CE MET 388	9.501 9.772 30.748 1.00 42.63
	ATOM	1768 C MET 388	8.385 12.746 35.849 1.00 33.41
15	ATOM	1769 O MET 388	8.573 13.934 36.103 1.00 42.63
	ATOM	1770 N LYS 389	7.235 12.126 36.092 1.00 39.26
	ATOM	1771 CA LYS 389	6.082 12.825 36.659 1.00 39.26
	ATOM	1772 CB LYS 389	4.867 11.900 36.719 1.00 52.87
	ATOM	1773 CG LYS 389	4.237 11.594 35.379 1.00 52.87
20	ATOM	1774 CD LYS 389	3.048 10.667 35.553 1.00 52.87
	ATOM	1775 CE LYS 389	3.482 9.327 36.125 1.00 52.87
	ATOM	1776 NZ LYS 389	2.335 8.407 36.326 1.00 52.87
	ATOM	1777 C LYS 389	6.363 13.360 38.056 1.00 39.26
	ATOM	1778 O LYS 389	5.837 14.404 38.452 1.00 52.87
25	ATOM	1779 N VAL 390	7.156 12.614 38.818 1.00 44.18 7.508 13.016 40.172 1.00 44.18
	ATOM	1780 CA VAL 390	8.299 11.898 40.905 1.00 50.50
	ATOM	1781 CB VAL 390 1782 CG1 VAL 390	8.718 12.362 42.293 1.00 50.50
	ATOM ATOM	1782 CG1 VAL 390 1783 CG2 VAL 390	7.455 10.640 41.012 1.00 50.50
20	ATOM	1784 C VAL 390	8.352 14.288 40.145 1.00 44.18
30	ATOM	1785 O VAL 390	8.144 15.198 40.948 1.00 50.50
	ATOM	1786 N GLU 391	9.261 14.368 39.179 1.00 38.64
	ATOM	1787 CA GLU 391	10.161 15.509 39.056 1.00 38.64
	ATOM	1788 CB GLU 391	11.483 15.060 38.424 1.00 64.18
35	ATOM	1789 CG GLU 391	12.065 13.766 39.009 1.00 64.18
	ATOM	1790 CD GLU 391	12.662 13.922 40.405 1.00 64.18
	ATOM	1791 OE1 GLU 391	12.190 14.773 41.192 1.00 64.18
	ATOM	1792 OE2 GLU 391	13.611 13.173 40.721 1.00 64.18
	ATOM	1793 C GLU 391	9.623 16.737 38.314 1.00 38.64
40	ATOM	1794 O GLU 391	9.656 17.850 38.849 1.00 64.18
	ATOM	1795 N CYS 392	9.125 16.539 37.096 1.00 37.24
	ATOM	1796 CA CYS 392	8.611 17.635 36.271 1.00 37.24
	ATOM	1797 CB CYS 392	8.879 17.345 34.784 1.00 30.64
	ATOM	1798 SG CYS 392	10.634 17.137 34.283 1.00 30.64
45	ATOM	1799 C CYS 392	7.110 17.882 36.496 1.00 37.24
	ATOM	1800 O CYS 392	6.403 17.011 37.006 1.00 30.64
	ATOM	1801 N PRO 393	6.625 19.107 36.199 1.00 40.56
	ATOM	1802 CD PRO 393	7.444 20.297 35.904 1.00 33.41
	ATOM	1803 CA PRO 393	5.209 19.473 36.358 1.00 40.56
50	ATOM	1804 CB PRO 393	5.253 21.001 36.404 1.00 33.41

6.409 21.332 35.527 1.00 33.41 ATOM 1805 CG PRO 393 ATOM 1806 C PRO 393 4.330 18.975 35.207 1.00 40.56 4.776 18.907 34.057 1.00 33.41 ATOM 1807 O PRO 393 3.067 18.691 35.516 1.00 41.91 ATOM 1808 N THR 394 2.101 18.186 34.540 1.00 41.91 ATOM 1809 CA THR 394 0.691 18.075 35.156 1.00 62.04 ATOM 1810 CB THR 394 0.706 18.582 36.497 1.00 62.04 ATOM 1811 OG1 THR 394 ATOM 1812 CG2 THR 394 0.232 16.626 35.168 1.00 62.04 ATOM 1813 C THR 394 1.995 18.984 33.242 1.00 41.91 1.758 18.411 32.181 1.00 62.04 ATOM 1814 O THR 394 10 2.191 20.297 33.327 1.00 43.92 ATOM 1815 N GLU 395 2.104 21.176 32.160 1.00 43.92 ATOM 1816 CA GLU 395 2.313 22.626 32.585 1.00 34.22 ATOM 1817 CB GLU 395 ATOM 1818 C GLU 395 3.071 20.814 31.031 1.00 43.92 2.887 21.243 29.891 1.00 34.22 ATOM 1819 O GLU 395 15 4.104 20.041 31.350 1.00 34.92 ATOM 1820 N LEU 396 5.096 19.634 30.359 1.00 34.92 ATOM 1821 CA LEU 396 ATOM 1822 CB LEU 396 6.473 19.495 31.017 1.00 35.81 7.074 20.747 31.662 1.00 35.81 ATOM 1823 CG LEU 396 8.427 20.410 32.263 1.00 35.81 ATOM 1824 CD1 LEU 396 20 7.209 21.857 30.629 1.00 35.81 ATOM 1825 CD2 LEU 396 4.731 18.324 29.661 1.00 34.92 ATOM 1826 C LEU 396 ATOM 1827 O LEU 396 5.343 17.954 28.659 1.00 35.81 ATOM 1828 N PHE 397 3.734 17.627 30.197 1.00 35.28 3.302 16.352 29.640 1.00 35.28 ATOM 1829 CA PHE 397 25 3.059 15.341 30.764 1.00 27.13 ATOM 1830 CB PHE 397 ATOM 1831 CG PHE 397 4.285 15.004 31.561 1.00 27.13 ATOM 1832 CD1 PHE 397 4.700 15.824 32.604 1.00 27.13 5.021 13.860 31.273 1.00 27.13 ATOM 1833 CD2 PHE 397 5.831 15.510 33.349 1.00 27.13 ATOM 1834 CE1 PHE 397 30 6.155 13.537 32.013 1.00 27.13 ATOM 1835 CE2 PHE 397 6.561 14.364 33.052 1.00 27.13 ATOM 1836 CZ PHE 397 2.027 16.474 28.812 1.00 35.28 ATOM 1837 C PHE 397 ATOM 1838 O PHE 397 0.977 16.861 29.331 1.00 27.13 ATOM 1839 N PRO 398 2.102 16.164 27.505 1.00 26.41 35 3.305 15.850 26.713 1.00 19.32 ATOM 1840 CD PRO 398 0.917 16.247 26.647 1.00 26.41 ATOM 1841 CA PRO 398 1,439 15.752 25.300 1.00 19.32 ATOM 1842 CB PRO 398 2.867 16.193 25.312 1.00 19.32 ATOM 1843 CG PRO 398 -0.157 15.313 27.206 1.00 26.41 ATOM 1844 C PRO 398 40 0.160 14.232 27.710 1.00 19.32 ATOM 1845 O PRO 398 -1.439 15.702 27.104 1.00 25.12 ATOM 1846 N PRO 399 -1.935 16.929 26.454 1.00 24.32 ATOM 1847 CD PRO 399 -2.554 14.894 27.612 1.00 25.12 ATOM 1848 CA PRO 399 -3.777 15.594 27.022 1.00 24.32 ATOM 1849 CB PRO 399 45 ATOM 1850 CG PRO 399 -3.349 17.026 26.974 1.00 24.32 -2.502 13.416 27.222 1.00 25.12 ATOM 1851 C PRO 399 -2.599 12.540 28.085 1.00 24.32 ATOM 1852 O PRO 399 ATOM 1853 N LEU 400 -2.322 13.139 25.933 1.00 23.10 ATOM 1854 CA LEU 400 -2.265 11.759 25.454 1.00 23.10 50

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-2.230 11.720 23.923 1.00 22.35
    ATOM 1855 CB LEU 400
                               -2.485 10.354 23.276 1.00 22.35
    ATOM 1856 CG LEU 400
                               -3.792 9.765 23.792 1.00 22.35
    ATOM 1857 CD1 LEU 400
                               -2.523 10.494 21.763 1.00 22.35
    ATOM 1858 CD2 LEU 400
                              -1.066 11.012 26.032 1.00 23.10
    ATOM 1859 C LEU 400
                               -1.160 9.825 26.345 1.00 22.35
    ATOM 1860 O LEU 400
    ATOM 1861 N PHE 401
                               0.044 11.723 26.202 1.00 13.85
                               1.269 11.150 26.755 1.00 13.85
    ATOM 1862 CA PHE 401
                                2.374 12.213 26.753 1.00 26.97
    ATOM 1863 CB PHE 401
                                3.729 11.702 27.164 1.00 26.97
    ATOM 1864 CG PHE 401
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                                4.189 10.461 26.732 1.00 26.97
    ATOM 1865 CD1 PHE 401
                                4.561 12.481 27.963 1.00 26.97
    ATOM 1866 CD2 PHE 401
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    ATOM 1867 CE1 PHE 401
                                5.830 12.035 28.327 1.00 26.97
    ATOM 1868 CE2 PHE 401
                                6.280 10.795 27.889 1.00 26.97
    ATOM 1869 CZ PHE 401
15
                               0.993 10.659 28.179 1.00 13.85
    ATOM 1870 C PHE 401
    ATOM 1871 O PHE 401
                               1.393 9.558 28.555 1.00 26.97
                               0.274 11.473 28.947 1.00 25.21
    ATOM 1872 N LEU 402
                               -0.080 11.145 30.325 1.00 25.21
    ATOM 1873 CA LEU 402
                               -0.640 12.380 31.035 1.00 29.34
    ATOM 1874 CB LEU 402
20
                                0.334 13.411 31.600 1.00 29.34
    ATOM 1875 CG LEU 402
    ATOM 1876 CD1 LEU 402
                                -0.430 14.658 32.018 1.00 29.34
                                1.090 12.814 32.775 1.00 29.34
    ATOM 1877 CD2 LEU 402
                               -1.109 10.025 30.425 1.00 25.21
    ATOM 1878 C LEU 402
                               -1.034 9.189 31.320 1.00 29.34
25
    ATOM 1879 O LEU 402
                               -2.090 10.043 29.529 1.00 23.54
    ATOM 1880 N GLU 403
    ATOM 1881 CA GLU 403
                                -3.159 9.046 29.521 1.00 23.54
                                -4.274 9.482 28.562 1.00 63.22
    ATOM 1882 CB GLU 403
                                -5.469 8.531 28.506 1.00 63.22
    ATOM 1883 CG GLU 403
                                -6.530 8.952 27.498 1.00 63.22
    ATOM 1884 CD GLU 403
30
                                -6.237 9.786 26.613 1.00 63.22
    ATOM 1885 OE1 GLU 403
                                -7.666 8.436 27.589 1.00 63.22
    ATOM 1886 OE2 GLU 403
                               -2.708 7.629 29.170 1.00 23.54
    ATOM 1887 C GLU 403
                               -3.210 6.656 29.735 1.00 63.22
    ATOM 1888 O GLU 403
                               -1.787 -7.515 28.221 1.00 33.24
    ATOM 1889 N VAL 404
35
                               -1.297 6.213 27.782 1.00 33.24
     ATOM 1890 CA VAL 404
                                -0.621 6.314 26.390 1.00 30.71
    ATOM 1891 CB VAL 404
                                -0.097 4.957 25.947 1.00 30.71
     ATOM 1892 CG1 VAL 404
                                -1.611 6.841 25.371 1.00 30.71
     ATOM 1893 CG2 VAL 404
     ATOM 1894 C VAL 404
                               -0.338 5.528 28.752 1.00 33.24
40
                               -0.386 4.305 28.914 1.00 30.71
     ATOM 1895 O VAL 404
                               0.526 6.309 29.392 1.00 33.66
     ATOM 1896 N PHE 405
                                1.516 5.752 30.308 1.00 33.66
     ATOM 1897 CA PHE 405
                                2.901 6.326 29.984 1.00 34.35
     ATOM 1898 CB PHE 405
                                3.343 6.076 28.568 1.00 34.35
     ATOM 1899 CG PHE 405
45
                                3.519 7.134 27.683 1.00 34.35
     ATOM 1900 CD1 PHE 405
     ATOM 1901 CD2 PHE 405
                                 3.569 4.782 28.114 1.00 34.35
                                3.911 6.906 26.365 1.00 34.35
     ATOM 1902 CE1 PHE 405
                                3.960 4.545 26.798 1.00 34.35
     ATOM 1903 CE2 PHE 405
                                4.131 5.610 25.922 1.00 34.35
     ATOM 1904 CZ PHE 405
50
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ATOM 1905 C PHE 405
                               1.189 5.931 31.790 1.00 33.66
                               2.036 5.539 32.623 1.00 34.35
     ATOM 1906 O PHE 405
                                 0.090 6.434 32.107 1.00 34.35
     ATOM 1907 OXT PHE 405
                              8.375 7.063 18.475 1.00 34.21
     ATOM 1908 C1 TRI
                              10.048 8.688 23.016 1.00 33.36
     ATOM 1909 C2 TRI
     ATOM 1910 C3 TRI
                              8.104 8.391 18.941 1.00 34.21
                         1
                              10.496 9.696 23.813 1.00 33.36
     ATOM 1911 C4 TRI
                          1
     ATOM 1912 C5 TRI
                              8.916 8.943 19.927 1.00 34.21
                          1
                              10.152 9.772 25.121 1.00 33.36
     ATOM 1913 C6 TRI
     ATOM 1914 C7 TRI
                              9.862 8.178 20.609 1.00 34.21
10
     ATOM 1915 C8 TRI
                              9.246 8.821 25.653 1.00 33.36
                              10.117 6.865 20.147 1.00 34.21
     ATOM 1916 C9 TRI
     ATOM 1917 C10 TRI
                              8.805 7.754 24.847 1.00 33.36
                          1
                               9.375 6.339 19.026 1.00 34.21
     ATOM 1918 C11 TRI
                          1
                               9.125 7.756 23.490 1.00 33.36
     ATOM 1919 C12 TRI
                          1
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     ATOM 1920 C13 TRI
                               8.158 6.555 15.938 1.00 35.85
     ATOM 1921 C15 TRI
                              8.713 10.990 20.395 1.00 34.21
     ATOM 1922 I1 TRI
                         1
     ATOM 1923 I2 TRI
                         1
                             10.951 11.289 26.315 1.00 33.36
                             11.592 5.685 21.118 1.00 34.21
     ATOM 1924 I3 TRI
20
                         1
                              9.407 6.654 15.852 1.00 35.85
     ATOM 1925 O3 TRI
                         1
     ATOM 1926 O2 TRI
                              10.570 8.649 21.717 1.00 33.36
                         1
     ATOM 1927 O1 TRI
                         1
                              8.798 8.969 26.979 1.00 33.36
     ATOM 1928 O4 TRI
                              7.352 6.522 14.973 1.00 35.85
                         1
     ATOM 1929 O1 HOH 501
                                9.189 2.098 11.091 1.00 33.36
25
                                 5.152 5.261 12.137 1.00 33.36
     ATOM 1930 O1 HOH 503
                                3.970 5.057 16.390 1.00 33.36
     ATOM 1931 O1 HOH 504
                                8.296 -0.941 8.998 1.00 33.36
     ATOM 1932 O1 HOH 534
     ATOM 1933 O1 HOH 538
                                4.845 14.369 13.635 1.00 33.36
                                 5.789 12.049 10.352 1.00 33.36
     ATOM 1934 O1 HOH 540
30
                                 5.721 2.525 28.939 1.00 33.36
     ATOM 1936 O1 HOH 555
                                3.732 1.273 26.724 1.00 33.36
     ATOM 1937 O1 HOH 556
                                 8.767 4.847 8.517 1.00 33.36
     ATOM 1935 O1 HOH 600
                                 1.863 1.579 0.837 1.00 37.00
     ATOM 1938 AS1 CAD 701
                                1.760 -0.100 0.335 1.00 33.36
     ATOM 1939 C2 CAD 701
35
                                3.511 1.872 1.858 1.00 28.02
     ATOM 1940 C3 CAD 701
     ATOM 1941 O4 CAD 701
                                1.785 2.506 -0.433 1.00 28.02
                                0.592 2.019 1.654 1.00 28.02
     ATOM 1942 O5 CAD 701
                               11.254 16.718 33.126 1.00 37.00
                                                              AS
     ATOM 1943 AS AS 801
                               16.338 -1.161 29.914 1.00 37.00
                                                              AS
     ATOM 1944 AS AS 802
     ATOM 1945 AS AS 803
                             -14.931 -11.763 25.324 1.00 37.00
                                                              AS
     END
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APPENDIX 5

TR IPBR2.PDB

REMARK rTR ipbr2 full length numbering

REMARK

REMARK Rfactor 0.214 Rfree 0.224

REMARK Resolution 15. 2.2 all reflections

REMARK

REMARK Three cacodylate-modified cysteines (CYA)

REMARK Cya334, Cya380, Cya392

REMARK cacodylate modeled as single arsenic atom 10

REMARK

REMARK side chain of certain residues modeled as ALA due to poor density;

REMARK however, residue name reflects true residue for clarity

15 REMARK

REMARK clone obtained from Murray et. al.

REMARK deposited sequence confirmed,

REMARK differing from that reported by Thompson et. al.

REMARK in the following codons:

REMARK 281 Thr - Ala 20

REMARK 285 Lys - Glu

REMARK identical to that reported by Mitsuhashi et. al.

REMARK gb:RNTRAVI X07409

JRNL

AUTH

M.B. MURRAY, N.D.ZILZ,

25 N.L.MCCREARY, M.J.MACDONALD

> JRNL **AUTH 2 H.C.TOWLE**

TITL ISOLATION AND CHARACTERIZATION OF RAT CDNA JRNL **CLONES FOR**

TWO

JRNL TITL 2 DISTINCT THYROID HORMONE RECPTORS 30

REF JBC JRNL

V. 263 25 1988 AUTH C.C.THOMPSON, C.WEINBERGER, R.LEBO, R.M.EVANS

JRNL TITL IDENTIFICATION OF A NOVEL THYROID HORMONE **JRNL**

RECEPTOR

EXPRESSED

TITL 2 IN THE MAMMALIAN CENTRAL NERVOUS SYSTEM JRNL

JRNL REF SCIENCE V. 237 1987

AUTH T.MITSUHASHI, G.TENNYSON, V.NIKODEM JRNL

TITL NUCLEOTIDE SEQUENCE OF NOVEL CDNAS GENERATED JRNL

40 BY

ALTERNATIVE

TITL 2 SPLICING OF A RAT THYROID HORMONE RECEPTOR JRNL GENE

TRANSCRIPT

REF NUC. ACIDS. RES. V. 16 12 1988 45 JRNL

REMARK

ATOM 1 CB ARG 157 68.481 10.663 6.906 1.00 57.50

69.793 10.213 7.512 1.00 59.93 ATOM 2 CG ARG 157

```
3 CD ARG 157
                               70.510 11.365 8.189 1.00 70.24
    ATOM
                              71.661 10.906 8.961 1.00 77.62
    ATOM
             4 NE ARG 157
             5 CZ ARG 157
                              71.599 10.492 10.224 1.00 78.75
    ATOM
                               70.440 10.480 10.870 1.00 74.33
             6 NH1 ARG 157
    ATOM
                               72.697 10.075 10.839 1.00 83.44
             7 NH2 ARG 157
    ATOM
                              66.314 10.014 5.809 1.00 46.84
             8 C ARG 157
    ATOM
                              66.109 10.397 4.659 1.00 54.49
             9 O ARG 157
    ATOM ·
                              68.442 9.069 5.013 1.00 56.54
             10 N ARG 157
    ATOM
                               67.704 9.537 6.222 1.00 52.92
    ATOM
             11 CA ARG 157
                              65.335 9.953 6.727 1.00 39.44
             12 N PRO 158
10
    ATOM
             13 CD PRO 158
                               65.503 9.448 8.099 1.00 41.72
    ATOM
                               63.946 10.368 6.487 1.00 34.98
             14 CA PRO 158
    ATOM
             15 CB PRO 158
                               63.282 10.172 7.854 1.00 34.92
    ATOM
                               64.096 9.096 8.487 1.00 45.83
             16 CG PRO 158
    ATOM
                              63.765 11.804 5.992 1.00 34.13
             17 C PRO 158
    ATOM
15
             18 O PRO 158
                              64.223 12.757 6.621 1.00 31.07
    ATOM
                              63.110 11.932 4.841 1.00 31.36
             19 N GLU 159
    ATOM
    ATOM
             20 CA GLU 159
                               62.814 13.220 4.228 1.00 27.34
             21 CB GLU 159
                               62.569 13.041 2.726 1.00 24.27
    ATOM
                               63.814 12.866 1.887 1.00 24.85
             22 CG GLU 159
20
    ATOM
                               64.409 14.188 1.454 1.00 28.12
             23 CD GLU 159
    ATOM
                               63.642 15.144 1.224 1.00 29.26
    ATOM
             24 OE1 GLU 159
                               65.646 14.269 1.326 1.00 29.52
    ATOM
             25 OE2 GLU 159
             26 C GLU 159
                              61.528 13.707 4.870 1.00 24.30
    ATOM
                              60.855 12.934 5.566 1.00 29.01
             27 O GLU 159
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     ATOM
                              61.192 14.989 4.718 1.00 24.62
             28 N PRO 160
    ATOM
                               61.979 16.126 4.188 1.00 18.72
     ATOM
             29 CD PRO 160
                               59.947 15.451 5.330 1.00 21.62
    ATOM
             30 CA PRO 160
                               59.945 16.955 5.048 1.00 12.71
             31 CB PRO 160
     ATOM
                               61.394 17.297 4.930 1.00 15.12
             32 CG PRO 160
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                              58.743 14.752 4.671 1.00 24.61
             33 C PRO 160
     ATOM
                              58.789 14.384 3.490 1.00 22.63
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             34 O PRO 160
                              57.705 14.504 5.450 1.00 25.86
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             35 N THR 161
                               56.515 13.864 4.921 1.00 23.77
             36 CA THR 161
     ATOM
                               55.689 13.201 6.048 1.00 21.75
             37 CB THR 161
     ATOM
35
                                55.178 14.210 6.926 1.00 20.78
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             38 OG1 THR 161
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             39 CG2 THR 161
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                              55.680 14.967 4.269 1.00 28.67
             40 C THR 161
     ATOM
                              55.917 16.151 4.510 1.00 29.90
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             41 O THR 161
                              54.685 14.597 3.448 1.00 27.79
             42 N PRO 162
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                               54.313 13.237 3.019 1.00 23.25
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             43 CD PRO 162
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             44 CA PRO 162
     ATOM
                               52.699 14.766 2.227 1.00 19.89
             45 CB PRO 162
     ATOM
                               53.394 13.492 1.848 1.00 20.63
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             46 CG PRO 162
                              53.334 16.661 3.775 1.00 24.81
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             47 C PRO 162
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                              53.477 17.863 3.526 1.00 21.10
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             49 N GLU 163
                              52.812 16.198 4.911 1.00 26.34
     ATOM
                               52.266 17.065 5.959 1.00 30.38
             50 CA GLU 163
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                               51.640 16.231 7.086 1.00 29.46
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             51 CB GLU 163
             52 CG GLU 163
                               50.482 15.321 6.666 1.00 48.37
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             54 OE1 GLU 163
             55 OE2 GLU 163
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                              53.353 17.949 6.552 1.00 26.74
             56 C GLU 163
    ATOM
                               53.109 19.107 6.898 1.00 27.03
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                               54.553 17.389 6.677 1.00 26.74
             58 N GLU 164
     ATOM
                               55.679 18.124 7.221 1.00 23.65
             59 CA GLU 164
    ATOM
                               56.805 17.174 7.609 1.00 18.85
             60 CB GLU 164
    ATOM
    ATOM
             61 CG GLU 164
                                56.441 16.306 8.804 1.00 26.81
                                57.536 15.334 9.188 1.00 31.06
             62 CD GLU 164
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                                58.404 15.050 8.340 1.00 29.21
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     ATOM
                                57.524 14.848 10.340 1.00 31.39
             64 OE2 GLU 164
    ATOM
             65 C GLU 164
                               56.165 19.204 6.276 1.00 26.54
     ATOM
             66 O GLU 164
                               56.609 20.258 6.724 1.00 32.48
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                              56.075 18.957 4.971 1.00 23.41
             67 N TRP 165
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                               56.488 19.962 3.998 1.00 20.81
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             68 CA TRP 165
                               56.462 19.405 2.573 1.00 18.15
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             69 CB TRP 165
    ATOM
             70 CG TRP 165
                               57.762 18.747 2.164 1.00 15.80
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             71 CD2 TRP 165
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             72 CE2 TRP 165
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                               59.527 20.676 2.287 1.00 17.56
             73 CE3 TRP 165
     ATOM
                                57.939 17.449 1.804 1.00 12.78
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             74 CD1 TRP 165
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             75 NEI TRP 165
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                               61.318 18.657 1.419 1.00 16.26
             76 CZ2 TRP 165
     ATOM
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             77 CZ3 TRP 165
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                                61.760 19.933 1.642 1.00 16.48
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             78 CH2 TRP 165
             79 C TRP 165
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     ATOM
             80 O TRP 165
                              55.975 22.295 3.960 1.00 23.61
     ATOM
                              54.269 20.882 4.376 1.00 22.66
             81 N ASP 166
     ATOM
             82 CA ASP 166
                              53.269 21.943 4.537 1.00 23.35
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     ATOM
                               51.863 21.359 4.716 1.00 22.61
     ATOM
             83 CB ASP 166
             84 CG ASP 166
                               51.347 20.681 3.458 1.00 31.41
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                                51.816 21.028 2.360 1.00 26.38
     ATOM
             85 OD1 ASP 166
             86 OD2 ASP 166
                                50.464 19.803 3.570 1.00 32.25
     ATOM
                              53.631 22.760 5.773 1.00 26.47
             87 C ASP 166
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     ATOM
                              53.694 23.991 5.718 1.00 30.25
             88 O ASP 166
     ATOM
                               53.887 22.054 6.872 1.00 24.12
             89 N LEU 167
     ATOM
     ATOM
                               54.268 22.663 8.139 1.00 26.44
             90 CA LEU 167
                               54.596 21.557 9.148 1.00 32.57
             91 CB LEU 167
     ATOM
                                54.659 21.919 10.629 1.00 36.97
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     ATOM
             92 CG LEU 167
                                53.289 22.402 11.080 1.00 43.83
             93 CD1 LEU 167
     ATOM
                                55.096 20.712 11.448 1.00 34.75
             94 CD2 LEU 167
     ATOM
                               55.501 23.533 7.904 1.00 23.19
             95 C LEU 167
     ATOM
                               55.570 24.670 8.368 1.00 28.18
             96 O LEU 167
     ATOM
             97 N ILE 168
                              56.450 22.988 7.147 1.00 19.25
45
     ATOM
                               57.703 23.651 6.801 1.00 17.71
     ATOM
             98 CA ILE 168
             99 CB ILE 168
                               58.632 22.693 6.006 1.00 14.43
     ATOM
                                59.740 23.451 5.304 1.00 16.71
     ATOM
             100 CG2 ILE 168
                                59.219 21.644 6.948 1.00 21.24
             101 CG1 ILE 168
     ATOM
            102 CD1 ILE 168
                               60.063 20.588 6.264 1.00 18.18
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57.475 24.931 6.002 1.00 28.73
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            103 C ILE 168
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    ATOM
            104 O ILE 168
                             56.601 24.866 5.005 1.00 24.43
            105 N HIS 169
    ATOM
                              56.319 26.027 4.169 1.00 23.64
            106 CA HIS 169
    ATOM
                              55.459 25.631 2.971 1.00 23.55
    ATOM
            107 CB HIS 169
                              56.140 24.683 2.034 1.00 23.82
    ATOM
            108 CG HIS 169
                              57.455 24.429 1.824 1.00 19.23
            109 CD2 HIS 169
    ATOM
            110 ND1 HIS 169
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                              56.302 23.089 0.522 1.00 19.56
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            111 CE1 HIS 169
            112 NE2 HIS 169
                              57.527 23.431 0.883 1.00 26.00
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    ATOM
                             55.653 27.135 4.962 1.00 19.37
    ATOM
            113 C HIS 169
                             56.069 28.288 4.880 1.00 25.64
    ATOM
            114 O HIS 169
            115 N VAL 170
                              54.638 26.782 5.745 1.00 19.88
    ATOM
                               53.925 27.758 6.555 1.00 20.28
    ATOM
            116 CA VAL 170
                               52.755 27.100 7.330 1.00 26.06
            117 CB VAL 170
    ATOM
15
                               52.093 28.109 8.259 1.00 20.15
            118 CG1 VAL 170
    ATOM
                               51.725 26.541 6.352 1.00 18.69
            119 CG2 VAL 170
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                              54.886 28.442 7.532 1.00 23.11
    ATOM
            120 C VAL 170
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            121 O VAL 170
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                              55.716 27.644 8.203 1.00 20.48
            122 N ALA 171
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                               56.686 28.146 9.173 1.00 19.84
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    ATOM
                               57.365 26.985 9.902 1.00 18.07
            124 CB ALA 171
    ATOM
    ATOM
            125 C ALA 171
                              57.728 29.049 8.512 1.00 20.62
            126 O ALA 171
                              58.033 30.127 9.037 1.00 24.67
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                              58.251 28.632 7.359 1.00 20.65
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            127 N THR 172
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            128 CA THR 172
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                               59.755 28.709 5.380 1.00 20.06
    ATOM
            129 CB THR 172
                               60.267 27.417 5.734 1.00 20.30
    ATOM
            130 OG1 THR 172
                               60.877 29.516 4.726 1.00 18.38
            131 CG2 THR 172
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                              58.675 30.786 6.235 1.00 24.43
            132 C THR 172
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    ATOM
                              59.346 31.815 6.360 1.00 23.54
           133 O THR 172
    ATOM
                              57.430 30.792 5.766 1.00 24.33
    ATOM
           134 N GLU 173
                               56.783 32.031 5.361 1.00 25.98
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            135 CA GLU 173
    ATOM 136 CB GLU 173
                               55.460 31.734 4.651 1.00 28.39
                               54.679 32.974 4.207 1.00 40.39
     ATOM 137 CG GLU 173
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            138 CD GLU 173
                               55.487 33.951 3.347 1.00 48.33
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                               55.261 35.172 3.478 1.00 51.86
     ATOM 139 OE1 GLU 173
                                56.334 33.513 2.533 1.00 46.92
            140 OE2 GLU 173
     ATOM
                              56.564 32.953 6.562 1.00 25.57
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            141 C GLU 173
                               56.877 34.141 6.498 1.00 27.76
            142 O GLU 173
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     ATOM
                               56.071 32.383 7.664 1.00 25.31
            143 N ALA 174
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                               55.823 33.128 8.900 1.00 22.66
            144 CA ALA 174
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                               55.340 32.183 10.000 1.00 18.21
            145 CB ALA 174
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                              57.097 33.847 9.338 1.00 23.47
            146 C ALA 174
     ATOM
                              57.056 35.003 9.755 1.00 23.76
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     ATOM
            147 O ALA 174
                              58.233 33.168 9.226 1.00 22.22
            148 N HIS 175
     ATOM
                              59.503 33.769 9.592 1.00 20.21
            149 CA HIS 175
     ATOM
                              60.586 32.700 9.738 1.00 13.82
            150 CB HIS 175
     ATOM
                              61.950 33.261 9.984 1.00 20.53
     ATOM
            151 CG HIS 175
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     ATOM 152 CD2 HIS 175
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            153 ND1 HIS 175
                               64.103 33.596 9.640 1.00 13.46
    ATOM
            154 CE1 HIS 175
                               63.715 34.410 10.605 1.00 20.86
            155 NE2 HIS 175
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                             59.949 34.822 8.571 1.00 25.39
    ATOM
           156 C HIS 175
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    ATOM
            157 O HIS 175
            158 N ARG 176
                               59.868 34.494 7.284 1.00 23.17
    ATOM
                               60.292 35.423 6.239 1.00 24.26
    ATOM 159 CA ARG 176
                               60.168 34.767 4.872 1.00 30.31
            160 CB ARG 176
    ATOM
    ATOM
            161 CG ARG 176
                               61.286 33.793 4.576 1.00 39.36
                               61.049 33.139 3.243 1.00 49.23
            162 CD ARG 176
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    ATOM
                               62.188 32.346 2.808 1.00 60.62
    ATOM
            163 NE ARG 176
                               62.230 31.688 1.653 1.00 67.96
    ATOM
            164 CZ ARG 176
            165 NH1 ARG 176
                                61.192 31.731 0.823 1.00 68.84
    ATOM
           166 NH2 ARG 176
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                              59.548 36.749 6.267 1.00 23.09
            167 C ARG 176
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                               60.163 37.807 6.173 1.00 30.71
    ATOM
            168 O ARG 176
                              58.240 36.686 6.488 1.00 22.69
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           169 N SER 177
    ATOM
           170 CA SER 177
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            171 CB SER 177
           172 OG SER 177
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            174 O SER 177
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            175 N THR 178
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            176 CA THR 178
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                               57.842 38.107 11.228 1.00 23.73
            177 CB THR 178
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    ATOM
                                58.354 36.776 11.337 1.00 24.26
    ATOM
            178 OG1 THR 178
            179 CG2 THR 178
                                56.344 38.037 10.994 1.00 16.77
    ATOM
            180 C THR 178
                              60.027 39.018 10.375 1.00 23.86
    ATOM
                               60.399 39.439 11.474 1.00 24.64
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                              60.873 38.690 9.402 1.00 23.79
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                               62.315 38.813 9.563 1.00 26.01
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            185 CG ASN 179
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            186 OD1 ASN 179
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                                65.364 37.516 8.432 1.00 35.34
            187 ND2 ASN 179
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                              62.767 40.101 8.875 1.00 32.11
            188 C ASN 179
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                              62.947 40.136 7.652 1.00 36.36
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            189 O ASN 179
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            191 CA ALA 180
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                               65.518 41.866 8.414 1.00 41.85
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            194 O ALA 180
                               64.266 43.163 7.057 1.00 37.15
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            195 N GLN 181
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            196 CA GLN 181
                               66.572 43.877 6.552 1.00 37.42
            197 CB GLN 181
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    ATOM
                               66.420 45.190 7.309 1.00 44.86
            198 CG GLN 181
    ATOM
                               65.779 46.285 6.479 1.00 53.60
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            199 CD GLN 181
                                64.712 46.793 6.821 1.00 58.51
     ATOM
            200 OEI GLN 181
     ATOM 201 NE2 GLN 181
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                               65.549 42.053 5.164 1.00 44.18
     ATOM 202 C GLN 181
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           205 CA GLY 182
                              65.074 39.713 4.732 1.00 46.26
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    ATOM 206 C GLY 182
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                              67.309 39.175 5.419 1.00 56.26
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                              66.907 39.274 3.205 1.00 50.96
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    ATOM 209 CA SER 183
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                              69.121 40.197 2.558 1.00 59.84
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                              70.352 40.138 2.540 1.00 66.02
                             68.453 41.338 2.413 1.00 60.68
    ATOM 214 N HIS 184
    ATOM 215 CA HIS 184
                              69.131 42.600 2.139 1.00 60.01
    ATOM 216 CB HIS 184
                              68.150 43.596 1.517 1.00 53.49
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                             70.373 44.300 3.303 1.00 59.56
    ATOM 218 O HIS 184
    ATOM 219 N TRP 185
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    ATOM 220 CA TRP 185
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    ATOM 221 CB TRP 185
    ATOM 222 CG TRP 185
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                               72.233 40.404 7.230 1.00 39.59
    ATOM 223 CD2 TRP 185
    ATOM 224 CE2 TRP 185
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                               73.202 41.146 7.919 1.00 35.23
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    ATOM 226 CD1 TRP 185
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    ATOM 227 NE1 TRP 185
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     ATOM 230 CH2 TRP 185
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                              72.605 42.584 4.938 1.00 54.57
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                              74.338 44.160 4.061 1.00 58.96
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                              75.417 44.731 4.226 1.00 62.57
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           237 O LYS 186
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                              73.382 44.640 3.268 1.00 60.12
     ATOM 238 N GLN 187
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     ATOM 239 CA GLN 187
                               73.157 45.653 1.050 1.00 57.00
    ATOM 240 CB GLN 187
                              72.809 47.064 3.101 1.00 60.91
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                              73.149 48.213 2.822 1.00 66.50
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                              71.795 46.790 3.919 1.00 59.55
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                               70.983 47.847 4.525 1.00 59.26
     ATOM 244 CA ARG 188
                               69.504 47.462 4.466 1.00 55.21
     ATOM 245 CB ARG 188
                              71.372 48.243 5.959 1.00 58.97
     ATOM 246 C ARG 188
                              70.914 49.269 6.469 1.00 58.54
     ATOM 247 O ARG 188
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     ATOM 248 N ARG 189
                              72.202 47.432 6.607 1.00 55.46
     ATOM 249 CA ARG 189
                               72.630 47.704 7.979 1.00 52.98
                               73.211 46.437 8.619 1.00 47.73
     ATOM 250 CB ARG 189
                               74.509 45.985 7.989 1.00 47.88
     ATOM 251 CG ARG 189
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     ATOM 252 CD ARG 189
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    ATOM 255 NH1 ARG 189
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    ATOM 256 NH2 ARG 189
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    ATOM 258 O ARG 189
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    ATOM 259 N LYS 190
                              7.4.444 50.722 9.435 1.00 48.83
    ATOM 260 CA LYS 190
    ATOM 261 CB LYS 190
                              73.682 52.036 9.516 1.00 45.36
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                              74.454 49.872 11.675 1.00 48.81
    ATOM 263 O LYS 190
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                              76.385 50.724 10.894 1.00 46.98
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    ATOM 266 CB PHE 191
                               78.630 50.520 11.873 1.00 44.25
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    ATOM 267 CG PHE 191
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    ATOM 268 CD1 PHE 191
                               78.828 49.124 9.791 1.00 52.20
                               80.029 48.437 11.748 1.00 47.25
    ATOM 269 CD2 PHE 191
    ATOM 270 CE1 PHE 191
                               79.335 48.031 9.090 1.00 55.86
    ATOM 271 CE2 PHE 191
                               80.542 47.343 11.059 1.00 49.73
                              80.195 47.139 9.727 1.00 51.55
    ATOM 272 CZ PHE 191
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                              76.764 51.443 13.233 1.00 46.44
    ATOM 273 C PHE 191
                              76.647 52.645 12.996 1.00 51.28
    ATOM 274 O PHE 191
    ATOM 275 N LEU 192
                              76.567 50.924 14.439 1.00 47.66
                               76.256 51.776 15.577 1.00 46.44
    ATOM 276 CA LEU 192
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    ATOM 277 CB LEU 192
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           278 CG LEU 192
    ATOM 279 CD1 LEU 192
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           280 CD2 LEU 192
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                              77.524 52.595 15.824 1.00 45.82
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    ATOM 285 CA PRO 193
                               78.560 54.836 15.999 1.00 47.34
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    ATOM 286 CB PRO 193
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    ATOM 287 CG PRO 193
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                              79.475 54.377 17.137 1.00 49.60
    ATOM 288 C PRO 193
                              79.000 54.033 18.218 1.00 54.05
    ATOM 289 O PRO 193
                              80.783 54.383 16.891 1.00 50.63
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    ATOM 291 CA ASP 194
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    ATOM 292 CB ASP 194
                               83.309 52.952 16.170 1.00 66.39
     ATOM 293 CG ASP 194
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     ATOM 294 OD1 ASP 194
                               83.640 51.787 16.486 1.00 69.00
     ATOM 295 OD2 ASP 194
                              81.769 54.726 19.198 1.00 54.41
     ATOM
           296 C ASP 194
                              82.229 54.221 20.222 1.00 55.27
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           297 O ASP 194
     ATOM
                              81.268 55.956 19.168 1.00 57.20
     ATOM 298 N ASP 195
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     ATOM 299 CA ASP 195
                               81.017 58.261 20.006 1.00 62.99
     ATOM 300 CB ASP 195
     ATOM 301 CG ASP 195
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    ATOM 305 O ASP 195
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    ATOM 309 CG2 ILE 196
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    ATOM 313 O ILE 196
                              78.912 52.570 21.298 1.00 42.07
                              78.357 53.228 23.370 1.00 45.62
    ATOM 314 N GLY 197
                               78.658 51.930 23.941 1.00 51.49
    ATOM 315 CA GLY 197
    ATOM 316 C GLY 197
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    ATOM 317 O GLY 197
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    ATOM 320 CB GLN 198
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    ATOM 322 O GLN 198
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    ATOM 326 OG SER 199
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    ATOM 331 CA PRO 200
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    ATOM 332 CB PRO 200
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    ATOM 334 C PRO 200
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    ATOM 335 O PRO 200
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    ATOM 338 CB ILE 201
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    ATOM 339 CG2 ILE 201
    ATOM 340 CG1 ILE 201
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    ATOM 341 CD1 ILE 201
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    ATOM 342 C ILE 201
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    ATOM 343 O ILE 201
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    ATOM 344 N VAL 202
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    ATOM 345 CA VAL 202
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    ATOM 346 CB VAL 202
    ATOM 347 CG1 VAL 202
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    ATOM 348 CG2 VAL 202
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    ATOM 349 C VAL 202
                              75.885 50.958 36.285 1.00 53.65
     ATOM 350 O VAL 202
                              75.914 50.010 35.500 1.00 55.10
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     ATOM 351 N SER 203
                               76.614 49.556 38.132 1.00 64.58
    ATOM 352 CA SER 203
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	ATOM	354 OG SER 203	78.396 50.523 39.483 1.00 74.02
	ATOM	355 C SER 203	75.493 48.528 38.197 1.00 61.69
	ATOM	356 O SER 203	74.351 48.846 38.535 1.00 63.63
5	ATOM	357 N MET 204	75.848 47.295 37.859 1.00 57.37
	ATOM	358 CA MET 204	74.932 46.162 37.885 1.00 57.54
	ATOM	359 CB MET 204	74.847 45.505 36.501 1.00 56.59
	ATOM	360 CG MET 204	74.012 46.270 35.489 1.00 44.08
	ATOM	361 SD MET 204	72.255 46.228 35.884 1.00 46.62
10	ATOM	362 CE MET 204	71.775 44.758 35.013 1.00 48.37
	ATOM	363 C MET 204	75.522 45.178 38.888 1.00 55.86
	ATOM	364 O MET 204	76.746 45.089 39.027 1.00 58.94
	ATOM	365 N PRO 205	74.671 44.432 39.607 1.00 55.36
	ATOM	366 CD PRO 205	73.203 44.570 39.625 1.00 57.73
15	ATOM	367 CA PRO 205	75.119 43.453 40.604 1.00 56.82
	ATOM	368 CB PRO 205	73.814 43.042 41.295 1.00 59.79
	ATOM	369 CG PRO 205	72.769 43.281 40.255 1.00 57.85
	ATOM	370 C PRO 205	75.902 42.239 40.083 1.00 57.25
	ATOM	371 O PRO 205	75.683 41.118 40.541 1.00 66.28
20	ATOM	372 N ASP 206	76.822 42.462 39.147 1.00 58.75
	ATOM	373 CA ASP 206	77.639 41.389 38.586 1.00 61.09
	ATOM	374 CB ASP 206	76.802 40.462 37.685 1.00 66.07
	ATOM	375 CG ASP 206	76.158 41.190 36.521 1.00 70.97
	ATOM	376 OD1 ASP 206	74.989 41.613 36.662 1.00 76.97
25	ATOM	377 OD2 ASP 206	76.813 41.322 35.465 1.00 61.12
	ATOM	378 C ASP 206	78.865 41.910 37.832 1.00 61.96
	ATOM	379 O ASP 206	79.406 41.230 36.957 1.00 65.14
	ATOM	380 N GLY 207	79.282 43.130 38.158 1.00 63.00
	ATOM	381 CA GLY 207	80.455 43.709 37.522 1.00 64.43
30	ATOM	382 C GLY 207	80.224 44.467 36.229 1.00 64.81
	ATOM	383 O GLY 207	80.649 45.619 36.110 1.00 68.76
	ATOM	384 N ASP 208	79.584 43.827 35.253 1.00 63.53
	ATOM	385 CA ASP 208	79.316 44.459 33.962 1.00 58.96
	ATOM	386 CB ASP 208	78.746 43.434 32.974 1.00 62.84
35	ATOM	387 CG ASP 208	79.743 42.336 32.633 1.00 64.73
	ATOM	388 OD1 ASP 208	79.575 41.200 33.121 1.00 66.65
	ATOM	389 OD2 ASP 208	80.701 42.610 31.878 1.00 68.91
	ATOM	390 C ASP 208	78.368 45.646 34.110 1.00 56.65
	ATOM	391 O ASP 208	77.182 45.473 34.392 1.00 55.79
40	ATOM	392 N LYS 209	78.911 46.852 33.953 1.00 54.66
	ATOM	393 CA LYS 209	78.132 48.081 34.082 1.00 53.92
	ATOM	394 CB LYS 209	79.034 49.236 34.515 1.00 49.71
	ATOM	395 C LYS 209	77.395 48.420 32.785 1.00 48.30
	ATOM	396 O LYS 209	77.767 47.945 31.711 1.00 45.62
45	ATOM	397 N VAL 210	76.367 49.258 32.894 1.00 43.87
	ATOM	398 CA VAL 210	75.539 49.662 31.757 1.00 41.25
	ATOM	399 CB VAL 210	74.020 49.624 32.125 1.00 32.99
	ATOM	400 CG1 VAL 210	73.153 50.029 30.937 1.00 31.44
_	ATOM	401 CG2 VAL 210	73.626 48.239 32.604 1.00 27.57
50	ATOM	402 C VAL 210	75.868 51.061 31.234 1.00 43.30

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	ATOM	403 O VAL 210	76.261 51.951 31.994 1.00 44.65
	ATOM	404 N ASP 211	75.688 51.235 29.931 1.00 43.23
	ATOM	405 CA ASP 211	75.906 52.498 29.240 1.00 40.62
	ATOM	406 CB ASP 211	76.686 52.232 27.943 1.00 43.49
5	ATOM	407 CG ASP 211	77.014 53.499 27.161 1.00 40.77
_	ATOM	408 OD1 ASP 211	76.180 54.427 27.092 1.00 42.13
	ATOM	409 OD2 ASP 211	78.111 53.549 26.574 1.00 37.49
	ATOM	410 C ASP 211	74.491 53.001 28.921 1.00 44.56
	ATOM	411 O ASP 211	73.849 52.500 27.998 1.00 46.44
10	ATOM	412 N LEU 212	74.006 53.982 29.684 1.00 43.76
	ATOM	413 CA LEU 212	72.662 54.538 29.494 1.00 41.47
	ATOM	414 CB LEU 212	72.473 55.785 30.359 1.00 40.45
	ATOM	415 CG LEU 212	72.360 55.585 31.867 1.00 44.47
	ATOM	416 CD1 LEU 212	72.127 56.923 32.551 1.00 40.49
15	ATOM	417 CD2 LEU 212	71.217 54.634 32.153 1.00 45.94
	ATOM	418 C LEU 212	72.325 54.886 28.049 1.00 40.77
	ATOM	419 O LEU 212	71.254 54.540 27.548 1.00 42.25
	ATOM	420 N GLU 213	73.241 55.588 27.394 1.00 42.53
	ATOM	421 CA GLU 213	73.068 56.008 26.009 1.00 43.60
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	ATOM	423 CG GLU 213	74.246 57.334 24.167 1.00 51.70
	ATOM	424 CD GLU 213	75.598 57.848 23.722 1.00 59.23
	ATOM	425 OE1 GLU 213	75.655 58.939 23.121 1.00 60.14
	ATOM	426 OE2 GLU 213	76.611 57.158 23.980 1.00 64.78
25	ATOM	427 C GLU 213	72.913 54.810 25.066 1.00 42.63
	ATOM	428 O GLU 213	72.008 54.779 24.226 1.00 37.04
	ATOM	429 N ALA 214	73.775 53.814 25.245 1.00 39.28
	ATOM	430 CA ALA 214	73.753 52.605 24.424 1.00 39.52
	ATOM	431 CB ALA 214	74.952 51.726 24.740 1.00 35.16
30	ATOM	432 C ALA 214	72.460 51.852 24.694 1.00 37.14
	ATOM	433 O ALA 214	71.795 51.390 23.767 1.00 42.29
	ATOM	434 N PHE 215	72.098 51.773 25.970 1.00 31.60
	ATOM	435 CA PHE 215	70.883 51.102 26.404 1.00 31.67
	ATOM	436 CB PHE 215	70.728 51.217 27.922 1.00 24.80
35	ATOM	437 CG PHE 215	69.512 50.522 28.458 1.00 21.78
	ATOM	438 CD1 PHE 215	69.553 49.171 28.771 1.00 24.64
	ATOM	439 CD2 PHE 215	68.328 51.223 28.658 1.00 21.53
	ATOM	440 CE1 PHE 215	68.429 48.528 29.277 1.00 27.63
	ATOM	441 CE2 PHE 215	67.200 50.591 29.163 1.00 21.60
40	ATOM	442 CZ PHE 215	67.249 49.242 29.472 1.00 21.35
	ATOM	443 C PHE 215	69.675 51.706 25.694 1.00 35.75
	ATOM	444 O PHE 215	68.838 50.975 25.161 1.00 34.84
	ATOM	445 N SER 216	69.604 53.035 25.665 1.00 39.09
	ATOM	446 CA SER 216	68.506 53.739 25.001 1.00 40.61
45	ATOM	447 CB SER 216	68.668 55.249 25.165 1.00 43.86
	ATOM	448 OG SER 216	68.616 55.603 26.537 1.00 68.66
	ATOM	449 C SER 216	68.444 53.380 23.518 1.00 40.76
	ATOM	450 O SER 216	67.362 53.161 22.969 1.00 35.50
	ATOM	451 N GLU 217	69.611 53.332 22.878 1.00 38.37
50	ATOM	452 CA GLU 217	69.709 52.989 21.462 1.00 37.80

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            454 CG GLU 217
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    ATOM
            455 CD GLU 217
                                70.881 55.315 19.925 1.00 53.25
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    ATOM
           456 OE1 GLU 217
                                70.920 55.056 18.702 1.00 57.12
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            457 OE2 GLU 217
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           458 C GLU 217
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    ATOM 459 O GLU 217
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            460 N PHE 218
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           461 CA PHE 218
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    ATOM 462 CB PHE 218
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            463 CG PHE 218
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    ATOM
            464 CD1 PHE 218
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                                71.510 48.233 21.163 1.00 23.53
            465 CD2 PHE 218
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                                73.504 48.072 23.073 1.00 27.68
    ATOM
           466 CE1 PHE 218
                                72.832 48.128 20.765 1.00 25.37
    ATOM
            467 CE2 PHE 218
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           468 CZ PHE 218
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                              67.445 49.202 22.321 1.00 31.30
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           469 C PHE 218
            470 O PHE 218
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            471 N THR 219
                               66.967 49.915 23.333 1.00 30.54
     ATOM
            472 CA THR 219
                                65.552 49.853 23.675 1.00 33.53
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                               65.269 50.467 25.057 1.00 36.07
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            473 CB THR 219
    ATOM
            474 OG1 THR 219
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            475 CG2 THR 219
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            477 O THR 219
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            479 CA LYS 220
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            480 CB LYS 220
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            481 C LYS 220
            482 O LYS 220
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            485 CB ILE 221
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            486 CG2 ILE 221
     ATOM
                               67.042 48.235 18.309 1.00 30.36
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     ATOM 488 CD1 ILE 221
     ATOM 489 C ILE 221
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     ATOM 490 O ILE 221
                              64.219 47.651 20.144 1.00 39.43
            491 N ILE 222
     ATOM
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            492 CA ILE 222
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            493 CB ILE 222
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            494 CG2 ILE 222
                               63.287 46.881 23.130 1.00 26.15
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     ATOM 495 CG1 ILE 222
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     ATOM 497 C ILE 222
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            498 O ILE 222
     ATOM 499 N THR 223
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     ATOM 500 CA THR 223
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    ATOM 511 C PRO 224
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    ATOM 513 N ALA 225
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    ATOM 515 CB ALA 225
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    ATOM 517 O ALA 225
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    ATOM 521 CG2 ILE 226
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    ATOM 522 CG1 ILE 226
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    ATOM 523 CD1 ILE 226
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    ATOM 524 C ILE 226
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    ATOM 525 O ILE 226
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    ATOM 527 CA THR 227
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    ATOM 528 CB THR 227
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    ATOM 529 OG1 THR 227
    ATOM 530 CG2 THR 227
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                              55.587 40.977 16.413 1.00 24.41
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     ATOM 535 CB ARG 228
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     ATOM 536 CG ARG 228
                               60.351 42.523 12.453 1.00 24.29
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                               61.641 42.168 13.047 1.00 27.04
     ATOM 538 NE ARG 228
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     ATOM 539 CZ ARG 228
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     ATOM 542 C ARG 228
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     ATOM 543 O ARG 228
     ATOM 544 N VAL 229
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     ATOM 545 CA VAL 229
                               59.149 37.707 18.524 1.00 17.21
     ATOM 546 CB VAL 229
                                59.023 36.322 19.152 1.00 13.73
     ATOM 547 CG1 VAL 229
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     ATOM 548 CG2 VAL 229
                               56.926 37.348 17.421 1.00 19.19
     ATOM 549 C VAL 229
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     ATOM 550 O VAL 229
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     ATOM 552 CA VAL 230
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553 CB VAL 230
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            554 CG1 VAL 230
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     ATOM
                                54.706 39.572 20.218 1.00 17.13
     ATOM
            555 CG2 VAL 230
            556 C VAL 230
                               54.003 37.707 16.902 1.00 26.39
     ATOM
            557 O VAL 230
                               53.180 36.790 16.843 1.00 29.63
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            558 N ASP 231
                              54.333 38.451 15.848 1.00 25.52
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                               53.724 38.242 14.537 1.00 26.78
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     ATOM
            560 CB ASP 231
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                               53.649 40.728 14.012 1.00 31.60
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            562 OD1 ASP 231
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                                54.271 41.727 13.593 1.00 35.74
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                              54.108 36.879 13.970 1.00 27.69
            564 C ASP 231
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     ATOM
            565 O ASP 231
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            566 N PHE 232
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            567 CA PHE 232
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            569 CG PHE 232
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            570 CD1 PHE 232
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     ATOM
            571 CD2 PHE 232
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            573 CE2 PHE 232
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                               58.561 30.893 13.873 1.00 26.10
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     ATOM
            575 C PHE 232
                              55.018 34.093 14.328 1.00 23.51
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                               51.997 34.305 15.760 1.00 30.19
            582 N LYS 234
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            584 CB LYS 234
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            586 CD LYS 234
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                               47.694 35.958 17.101 1.00 59.60
            587 CE LYS 234
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     ATOM
            588 NZ LYS 234
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            597 NZ LYS 235
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     ATOM
            598 C LYS 235
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            599 O LYS 235
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            600 N LEU 236
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            601 CA LEU 236
     ATOM
     ATOM 602 CB LEU 236
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                               49.104 26.126 14.860 1.00 45.79
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            616 CA MET 238
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                               50.133 24.505 16.378 1.00 49.72
            617 CB MET 238
    ATOM
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                               51.342 22.205 15.284 1.00 60.11
    ATOM 619 SD MET 238
                               50.993 21.626 13.625 1.00 53.03
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           620 CE MET 238
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            621 C MET 238
                               49.103 26.593 17.324 1.00 53.36
                               48.583 26.365 18.420 1.00 58.87
    ATOM 622 O MET 238
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            624 CA PHE 239
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                               51.011 29.736 17.677 1.00 32.92
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     ATOM 626 CG PHE 239
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            627 CD1 PHE 239
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            628 CD2 PHE 239
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            630 CE2 PHE 239
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            631 CZ PHE 239
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            633 O PHE 239
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                              47.958 30.166 17.321 1.00 36.32
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            634 N SER 240
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            635 CA SER 240
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            636 CB SER 240
                               47.390 32.671 15.947 1.00 52.67
            637 OG SER 240
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     ATOM
                               44.548 30.743 18.485 1.00 43.02
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            639 O SER 240
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                                44.554 27.954 18.408 1.00 40.35
            641 CA GLU 241
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                                44.788 26.521 17.926 1.00 49.38
            642 CB GLU 241
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                                44.541 26.287 16.452 1.00 65.25
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            643 CG GLU 241
                                44.873 24.856 16.002 1.00 70.72
            644 CD GLU 241
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                                44.806 23.923 16.845 1.00 73.36
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            645 OE1 GLU 241
                                45.211 24.679 14.805 1.00 68.60
     ATOM 646 OE2 GLU 241
                               44,550 27.968 19.934 1.00 37.83
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            647 C GLU 241
            648 O GLU 241
                               43.504 27.857 20.570 1.00 40.77
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                               45.747 28.103 20.498 1.00 34.71
     ATOM 649 N LEU 242
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            650 CA LEU 242
     ATOM
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            651 CB LEU 242
     ATOM
                               48.345 27.006 22.455 1.00 30.51
     ATOM 652 CG LEU 242
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            654 CD2 LEU 242
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    ATOM
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                              45.274 29.287 22.657 1.00 29.41
                              45.029 30.339 22.071 1.00 28.12
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           657 N PRO 243
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    ATOM 659 CA PRO 243
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                               45.621 33.749 24.931 1.00 45.78
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    ATOM 666 CB CYS 244
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                               44.068 35.680 23.580 1.00100.76
    ATOM 667 SG CYS 244
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    ATOM 670 O CYS 244
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    ATOM 673 CB GLU 245
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    ATOM 674 CG GLU 245
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    ATOM 675 CD GLU 245
                                43.080 32.693 30.618 1.00 38.31
    ATOM 676 OE1 GLU 245
    ATOM 677 OE2 GLU 245
                                43.697 32.644 28.516 1.00 48.13
    ATOM 678 C GLU 245
                               48.376 32.109 27.984 1.00 29.54
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                               49.497 32.437 28.381 1.00 33.54
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                              48.146 31.034 27.236 1.00 26.40
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           682 CB ASP 246
                               48.650 28.887 26.153 1.00 29.86
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                               48.184 27.876 27.175 1.00 34.10
    ATOM 683 CG ASP 246
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    ATOM 684 OD1 ASP 246
                                47.863 26.742 26.772 1.00 35.79
     ATOM 685 OD2 ASP 246
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                              51.331 30.789 25.863 1.00 27.35
     ATOM 687 O ASP 246
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     ATOM 689 CA GLN 247
                               49.228 33.089 22.924 1.00 23.38
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           690 CB GLN 247
     ATOM 691 CG GLN 247
                               48.303 32.213 22.091 1.00 23.76
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     ATOM 692 CD GLN 247
                                47.853 34.054 20.628 1.00 33.51
           693 OE1 GLN 247
     ATOM
     ATOM 694 NE2 GLN 247
                                46.198 32.593 20.957 1.00 27.44
     ATOM 695 C GLN 247
                               51.133 33.313 24.511 1.00 22.74
                               52.326 33.373 24.205 1.00 27.63
           696 O GLN 247
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                              50.588 34.047 25.473 1.00 25.03
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           699 CB ILE 248
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            700 CG2 ILE 248
     ATOM
            701 CG1 ILE 248
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     ATOM 703 C ILE 248 52.535 34.382 26.939 1.00 27.53
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    ATOM
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            706 CA ILE 249
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                              52.759 31.395 29.166 1.00 29.81
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            707 CB ILE 249
            708 CG2 ILE 249
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            709 CG1 ILE 249
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                               51.173 30.838 31.076 1.00 32.35
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                               54.303 30.224 24.214 1.00 23.75
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            716 CG LEU 250
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           717 CD1 LEU 250
    ATOM
            718 CD2 LEU 250
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            721 N LEU 251
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            722 CA LEU 251
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            723 CB LEU 251
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                                53.121 36.217 21.939 1.00 35.03
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            725 CD1 LEU 251
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            726 CD2 LEU 251
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                               61.572 31.948 26.489 1.00 31.90
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            743 CA CYS 254
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                               58.976 32.310 21.909 1.00 24.24
            745 SG CYS 254
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                               61.353 33.716 23.164 1.00 22.79
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                               62.217 33.683 22.282 1.00 23.23
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            749 CA CYS 255
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            753 O CYS 255
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            756 CB MET 256
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                                66.781 37.094 25.272 1.00 17.41
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            758 SD MET 256
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            759 CE MET 256
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                                65.085 31.989 22.753 1.00 24.00
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            777 C ILE 258
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                              65.605 35.263 17.484 1.00 22.58
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            780 CA MET 259
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            783 SD MET 259
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            792 O SER 260
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                                67.739 32.608 17.053 1.00 22.66
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                                67.719 31.759 15.781 1.00 22.12
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            796 CG LEU 261
            797 CD1 LEU 261
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                                66,498 30.851 15.800 1.00 19.60
            798 CD2 LEU 261
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            799 C LEU 261
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     ATOM 803 CB ARG 262
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	ATOM	804 CG ARG 262	65.304 36.268 14.362 1.00 21.48
•	ATOM	805 CD ARG 262	64.026 37.077 14.345 1.00 19.12
	ATOM	806 NE ARG 262	62.990 36.377 13.599 1.00 22.18
	ATOM	807 CZ ARG 262	61.780 36.862 13.333 1.00 22.88
5	ATOM	808 NH1 ARG 262	61.429 38.075 13.752 1.00 20.81
	ATOM	809 NH2 ARG 262	60.912 36.129 12.648 1.00 20.26
	ATOM	810 C ARG 262	69.044 37.196 14.531 1.00 25.05
	ATOM	811 O ARG 262	69.485 37.513 13.427 1.00 22.98
	ATOM	812 N ALA 263	69.608 37.579 15.676 1.00 26.36
10	ATOM	813 CA ALA 263	70.818 38.400 15.705 1.00 27.02
	ATOM	814 CB ALA 263	70.997 39.045 17.087 1.00 25.80
	ATOM	815 C ALA 263	72.026 37.514 15.368 1.00 25.21
	ATOM	816 O ALA 263	72.825 37.844 14.492 1.00 31.14
	ATOM	817 N ALA 264	72.109 36.358 16.027 1.00 25.62
15	ATOM	818 CA ALA 264	73.203 35.408 15.828 1.00 23.85
13	ATOM	819 CB ALA 264	73.062 34.237 16.794 1.00 17.15
	ATOM	820 C ALA 264	73.345 34.901 14.391 1.00 26.03
	ATOM	821 O ALA 264	74.460 34.773 13.886 1.00 25.66
	ATOM	822 N VAL 265	72.234 34.615 13.723 1.00 25.22
20	ATOM	823 CA VAL 265	72.327 34.128 12.350 1.00 28.38
20	ATOM	824 CB VAL 265	71.028 33.457 11.857 1.00 24.59
	ATOM	825 CG1 VAL 265	70.707 32.264 12.719 1.00 25.53
	ATOM	826 CG2 VAL 265	69.881 34.440 11.853 1.00 20.86
	ATOM	827 C VAL 265	72.747 35.235 11.393 1.00 31.46
25	ATOM	828 O VAL 265	73.024 34.973 10.222 1.00 34.75
23	ATOM	829 N ARG 266	72.795 36.464 11.896 1.00 30.10
	ATOM	830 CA ARG 266	73.211 37.602 11.089 1.00 30.69
	ATOM	831 CB ARG 266	72.170 38.713 11.148 1.00 25.13
	ATOM	832 CG ARG 266	70.976 38.406 10.299 1.00 25.43
30	ATOM	833 CD ARG 266	69.999 39.537 10.277 1.00 29.56
50	ATOM	834 NE ARG 266	69.032 39.340 9.205 1.00 31.59
	ATOM	835 CZ ARG 266	67.814 39.861 9.197 1.00 31.18
	ATOM	836 NH1 ARG 266	67.408 40.611 10.215 1.00 31.01
	ATOM	837 NH2 ARG 266	67.012 39.648 8.163 1.00 28.21
35	ATOM	838 C ARG 266	74.568 38.111 11.544 1.00 34.28
55	ATOM	839 O ARG 266	74.877 39.300 11.423 1.00 41.19
	ATOM	840 N TYR 267	75.362 37.207 12.108 1.00 30.80
	ATOM	841 CA TYR 267	76.694 37.544 12.573 1.00 33.84
	ATOM	842 CB TYR 267	
40	ATOM	843 CG TYR 267	78.674 36.570 13.867 1.00 34.23
	ATOM	844 CD1 TYR 267	79.131 37.465 14.835 1.00 32.60
	ATOM	845 CE1 TYR 267	80.491 37.593 15.106 1.00 34.90
	ATOM	846 CD2 TYR 267	79.615 35.801 13.184 1.00 32.84
	ATOM	847 CE2 TYR 267	80.972 35.920 13.446 1.00 34.70
45	ATOM	848 CZ TYR 267	81.404 36.816 14.405 1.00 36.21
7.7	ATOM	849 OH TYR 267	82.749 36.940 14.651 1.00 39.48
	ATOM	850 C TYR 267	77.615 37.649 11.360 1.00 37.82
	ATOM	851 O TYR 267	77.648 36.749 10.517 1.00 39.45
	ATOM	852 N ASP 268	78.319 38.769 11.239 1.00 44.62
50	ATOM	853 CA ASP 268	79.248 38.963 10.133 1.00 45.56
	1110111	000 011 1101 -00	

	ATOM	854 CB ASP 268	79.096 40.366 9.533 1.00 46.62
	ATOM	855 CG ASP 268	80.068 40.624 8.391 1.00 50.96
	ATOM	856 OD1 ASP 268	80.204 39.755 7.502 1.00 55.65
	ATOM	857 OD2 ASP 268	80.700 41.699 8.384 1.00 52.09
5	ATOM	858 C ASP 268	80.675 38.751 10.630 1.00 44.44
	ATOM	859 O ASP 268	81.242 39.614 11.304 1.00 45.68
	ATOM	860 N PRO 269	81.281 37.600 10.296 1.00 45.94
	ATOM	861 CD PRO 269	80.739 36.503 9.476 1.00 43.72
	MOTA	862 CA PRO 269	82.651 37.309 10.730 1.00 46.63
10	ATOM	863 CB PRO 269	82.884 35.889 10.208 1.00 43.88
	ATOM	864 CG PRO 269	81.983 35.797 9.018 1.00 44.66
	ATOM	865 C PRO 269	83.682 38.298 10.190 1.00 50.80
	ATOM	866 O PRO 269	84.681 38.578 10.854 1.00 48.56
	ATOM	867 N ALA 270	83.407 38.858 9.012 1.00 55.09
15	ATOM	868 CA ALA 270	84.306 39.820 8.374 1.00 55.68
	ATOM	869 CB ALA 270	83.799 40.168 6.974 1.00 53.64
	ATOM	870 C ALA 270	84.528 41.096 9.196 1.00 56.18
	ATOM	871 O ALA 270	85.577 41.729 9.082 1.00 61.07
	ATOM	872 N SER 271	83.543 41.479 10.006 1.00 51.38
20	ATOM	873 CA SER 271	83.661 42.678 10.836 1.00 45.90
	ATOM	874 CB SER 271	82.710 43.774 10.346 1.00 44.49
	ATOM	875 OG SER 271	81.360 43.358 10.404 1.00 45.26
	ATOM	876 C SER 271	83.409 42.395 12.317 1.00 46.61
	ATOM	877 O SER 271	83.431 43.309 13.143 1.00 48.31
25	ATOM	878 N ASP 272	83.172 41.126 12.642 1.00 46.73
	ATOM	879 CA ASP 272	82.920 40.689 14.013 1.00 42.49
	ATOM	880 CB ASP 272	84.200 40.807 14.849 1.00 42.12
	ATOM	881 CG ASP 272	84.103 40.072 16.169 1.00 50.30
20	ATOM	882 OD1 ASP 272	83.417 39.028 16.218 1.00 45.10
30	ATOM	883 OD2 ASP 272	84.708 40.537 17.160 1.00 57.61
	ATOM	884 C ASP 272	81.769 41.465 14.658 1.00 40.95 81.885 41.975 15.779 1.00 42.93
	ATOM	885 O ASP 272	80.651 41.531 13.945 1.00 38.57
	ATOM ATOM	886 N THR 273 887 CA THR 273	79.473 42.239 14.425 1.00 40.99
25	_	888 CB THR 273	79.262 43.574 13.656 1.00 40.76
35	ATOM ATOM	889 OG1 THR 273	79.240 43.318 12.248 1.00 42.61
	ATOM	890 CG2 THR 273	80.373 44.574 13.965 1.00 39.67
	ATOM	891 C THR 273	78.210 41.397 14.251 1.00 39.94
	ATOM	892 O THR 273	78.202 40.419 13.494 1.00 36.66
40	ATOM	893 N LEU 274	77.168 41.757 14.993 1.00 36.08
40	ATOM	894 CA LEU 274	75.867 41.096 14.907 1.00 34.28
	ATOM	895 CB LEU 274	75.343 40.699 16.292 1.00 30.96
	ATOM	896 CG LEU 274	75.952 39.536 17.068 1.00 30.19
	ATOM	897 CD1 LEU 274	75.310 39.472 18.444 1.00 26.29
45	ATOM	898 CD2 LEU 274	75.744 38.237 16.309 1.00 27.43
73	ATOM	899 C LEU 274	74.943 42.163 14.347 1.00 36.49
	ATOM	900 O LEU 274	75.152 43.354 14.596 1.00 40.27
	ATOM	901 N THR 275	73.923 41.758 13.606 1.00 36.42
	ATOM	902 CA THR 275	72.994 42.731 13.062 1.00 35.07
50	ATOM	903 CB THR 275	72.773 42.522 11.556 1.00 36.04
20	111 0111	, 55 OD 1111C 275	

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904 OG1 THR 275
                                74.028 42.625 10.875 1.00 41.52
    ATOM
                               71.852 43.583 11.008 1.00 36.47
            905 CG2 THR 275
    ATOM
                              71.673 42.655 13.814 1.00 34.32
    ATOM
            906 C THR 275
            907 O THR 275
                              71.055 41.590 13.907 1.00 34.96
    ATOM
                              71.292 43.767 14.432 1.00 31.79
            908 N LEU 276
    ATOM
                               70.044 43.840 15.173 1.00 29.47
            909 CA LEU 276
    ATOM
                               70.181 44.766 16.389 1.00 25.29
            910 CB LEU 276
    ATOM
            911 CG LEU 276
                               71.328 44.501 17.383 1.00 29.01
    ATOM
                               71.179 45.410 18.594 1.00 20.92
    ATOM 912 CD1 LEU 276
                               71.358 43.042 17.834 1.00 22.79
10
    ATOM 913 CD2 LEU 276
                              68.966 44.350 14.228 1.00 31.69
           914 C LEU 276
    ATOM
                              69.175 45.335 13.510 1.00 33.87
            915 O LEU 276
    ATOM
    ATOM
            916 N SER 277
                              67.862 43.608 14.162 1.00 33.07
            917 CA SER 277
                               66.721 43.935 13.315 1.00 30.61
    ATOM
           918 CB SER 277
                               65.949 45.111 13.909 1.00 22.87
    ATOM
15
                               65.587 44.822 15.250 1.00 23.35
    ATOM 919 OG SER 277
                              67.103 44.200 11.860 1.00 31.85
    ATOM 920 C SER 277
                              66.433 44.958 11.158 1.00 32.13
    ATOM 921 O SER 277
    ATOM
            922 N GLY 278
                              68.188 43.566 11.421 1.00 32.29
            923 CA GLY 278
                               68.664 43.716 10.058 1.00 37.59
20
    ATOM
            924 C GLY 278
                              69.063 45.122 9.639 1.00 43.26
    ATOM
                              69.313 45.358 8.455 1.00 42.60
            925 O GLY 278
    ATOM
                              69.177 46.038 10.599 1.00 43.42
    ATOM
            926 N GLU 279
                               69.532 47.420 10.291 1.00 44.55
            927 CA GLU 279
    ATOM
            928 CB GLU 279
                               68.292 48.310 10.394 1.00 44.66
25
    ATOM
                               67.671 48.344 11.783 1.00 54.19
            929 CG GLU 279
    ATOM
                               66.400 49.171 11.845 1.00 64.96
            930 CD GLU 279
    ATOM
                               65.627 49.174 10.859 1.00 71.43
    ATOM
            931 OE1 GLU 279
            932 OE2 GLU 279
                                66.167 49.814 12.891 1.00 66.65
    ATOM
                              70.654 48.019 11.133 1.00 45.52
30
    ATOM
            933 C GLU 279
                              71.207 49.057 10.772 1.00 51.83
            934 O GLU 279
    ATOM
                               71.007 47.373 12.242 1.00 44.66
    ATOM
            935 N MET 280
                               72.060 47.904 13.105 1.00 34.22
            936 CA MET 280
    ATOM
            937 CB MET 280
                               71.470 48.382 14.433 1.00 32.38
    ATOM
            938 CG MET 280
                               72.479 49.058 15.345 1.00 37.87
    ATOM
35
                               71.912 49.201 17.052 1.00 41.78
    ATOM
            939 SD MET 280
                               70.650 50.495 16.911 1.00 37.01
    ATOM
            940 CE MET 280
                              73.183 46.920 13.386 1.00 35.70
            941 C MET 280
    ATOM
    ATOM
            942 O MET 280
                               72.976 45.900 14.044 1.00 36.99
                              74.366 47.221 12.867 1.00 34.80
            943 N ALA 281
40
    ATOM
                               75.535 46.377 13.091 1.00 35.11
    ATOM
           944 CA ALA 281
                               76.529 46.527 11.955 1.00 31.27
            945 CB ALA 281
    ATOM
                              76.155 46.837 14.406 1.00 35.96
           946 C ALA 281
     ATOM
                               76.478 48.015 14.570 1.00 39.10
     ATOM 947 O ALA 281
                               76.285 45.916 15.353 1.00 36.46
     ATOM 948 N VAL 282
45
     ATOM 949 CA VAL 282
                               76.839 46.246 16.655 1.00 36.05
                               75.783 46.090 17.783 1.00 35.60
     ATOM 950 CB VAL 282
                                74.633 47.069 17.568 1.00 38.73
     ATOM 951 CG1 VAL 282
                                75.262 44.660 17.844 1.00 33.27
     ATOM 952 CG2 VAL 282
                              78.062 45.408 16.996 1.00 37.70
50
     ATOM 953 C VAL 282
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	ATOM	954 O VAL 282	78.137 44.223 16.660 1.00 37.45
	ATOM	955 N ALA 283	79.032 46.047 17.637 1.00 39.21
	ATOM	956 CA ALA 283	80.254 45.375 18.048 1.00 43.73
	ATOM	957 CB ALA 283	81.433 46.352 18.047 1.00 42.04
5	ATOM	958 C ALA 283	80.060 44.752 19.435 1.00 43.28
	ATOM	959 O ALA 283	79.179 45.157 20.203 1.00 45.77
	ATOM	960 N ARG 284	80.903 43.774 19.744 1.00 41.96
	ATOM	961 CA ARG 284	80.866 43.044 21.004 1.00 44.87
	ATOM	962 CB ARG 284	82.084 42.125 21.087 1.00 46.34
10	ATOM	963 CG ARG 284	81.930 40.947 22.017 1.00 51.85
	ATOM	964 CD ARG 284	83.107 40.010 21.844 1.00 60.73
	ATOM	965 NE ARG 284	83.262 39.571 20.455 1.00 54.30
	ATOM	966 CZ ARG 284	83.221 38.300 20.074 1.00 53.66
	ATOM	967 NH1 ARG 284	83.032 37.343 20.973 1.00 49.99
15	ATOM	968 NH2 ARG 284	83.379 37.984 18.797 1.00 47.31
	ATOM	969 C ARG 284	80.803 43.945 22.237 1.00 44.85
	ATOM	970 O ARG 284	79.896 43.806 23.062 1.00 48.26
	ATOM	971 N GLU 285	81.750 44.873 22.349 1.00 41.60
	ATOM	972 CA GLU 285	81.802 45.787 23.484 1.00 41.17
20	ATOM	973 CB GLU 285	83.043 46.675 23.392 1.00 39.97
	ATOM	974 C GLU 285	80.538 46.640 23.603 1.00 40.08
	ATOM	975 O GLU 285	80.023 46.849 24.703 1.00 41.16
	ATOM	976 N GLN 286	80.017 47.088 22.463 1.00 38.49
	ATOM	977 CA GLN 286	78.818 47.926 22.425 1.00 36.25
25	ATOM	978 CB GLN 286	78.549 48.401 20.997 1.00 39.50
	ATOM	979 CG GLN 286	79.619 49.311 20.424 1.00 43.62
	ATOM	980 CD GLN 286	79.324 49.710 18.987 1.00 49.48
	ATOM	981 OE1 GLN 286	79.253 48.856 18.097 1.00 48.41
	ATOM	982 NE2 GLN 286	79.125 51.000 18.755 1.00 47.15
30	ATOM	983 C GLN 286	77.563 47.255 22.988 1.00 35.40
	ATOM	984 O GLN 286	76.903 47.806 23.871 1.00 31.24
	ATOM	985 N LEU 287	77.234 46.071 22.480 1.00 32.96
	ATOM	986 CA LEU 287	76.055 45.349 22.950 1.00 33.40
	ATOM	987 CB LEU 287	75.767 44.138 22.054 1.00 28.67
35	ATOM	988 CG LEU 287	74.466 43.375 22.342 1.00 26.66
	ATOM	989 CD1 LEU 287	73.263 44.305 22.244 1.00 19.41
	ATOM	990 CD2 LEU 287	74.325 42.221 21.368 1.00 24.84
	ATOM	991 C LEU 287	76.234 44.914 24.406 1.00 34.81
	ATOM	992 O LEU 287	75.265 44.857 25.175 1.00 33.92
40	ATOM	993 N LYS 288	77.476 44.621 24.781 1.00 35.38
	ATOM	994 CA LYS 288	77.814 44.204 26.140 1.00 36.12
	ATOM	995 CB LYS 288	79.296 43.839 26.210 1.00 37.13
	ATOM	996 CG LYS 288	79.762 43.280 27.533 1.00 44.61
	ATOM	997 CD LYS 288	81.256 43.018 27.494 1.00 54.07
45	ATOM	998 CE LYS 288	81.757 42.435 28.801 1.00 60.87
	ATOM	999 NZ LYS 288	81.291 41.041 29.039 1.00 61.53
	ATOM		77.510 45.345 27.109 1.00 36.90
	ATOM		76.684 45.206 28.013 1.00 40.68
	ATOM		78.129 46.495 26.863 1.00 35.94
50	ATOM	1003 CA ASN 289	77.947 47.680 27.695 1.00 36.12

	ATOM	1004 CB ASN 289	78.982 48.738 27.332 1.00 31.78
	ATOM	1005 CG ASN 289	80.388 48.263 27.569 1.00 40.31
	ATOM	1006 OD1 ASN 289	80.627 47.422 28.440 1.00 43.12
	ATOM	1007 ND2 ASN 289	81.326 48.758 26.775 1.00 35.36
5	ATOM	1008 C ASN 289	76.553 48.277 27.590 1.00 36.98
	ATOM	1009 O ASN 289	76.099 48.959 28.509 1.00 34.29
	ATOM	1010 N GLY 290	75.883 48.032 26.466 1.00 32.65
	ATOM	1011 CA GLY 290	74.541 48.550 26.256 1.00 28.61
	ATOM	1012 C GLY 290	73.497 48.001 27.210 1.00 26.54
10	ATOM	1013 O GLY 290	72.362 48.480 27.234 1.00 31.06
	ATOM	1014 N GLY 291	73.861 46.978 27.977 1.00 28.89
	ATOM	1015 CA GLY 291	72.929 46.413 28.937 1.00 25.24
	ATOM	1016 C GLY 291	72.872 44.900 28.997 1.00 28.12
	ATOM	1017 O GLY 291	72.335 44.345 29.955 1.00 31.16
15	ATOM	1018 N LEU 292	73.406 44.223 27.985 1.00 29.51
	ATOM	1019 CA LEU 292	73.361 42.766 27.969 1.00 32.79
	ATOM	1020 CB LEU 292	73.304 42.240 26.531 1.00 28.00
	ATOM	1021 CG LEU 292	71.948 42.355 25.827 1.00 23.68
	ATOM	1022 CD1 LEU 292	72.004 41.626 24.509 1.00 26.12
20	ATOM	1023 CD2 LEU 292	70.851 41.764 26.694 1.00 23.36
	ATOM	1024 C LEU 292 1025 O LEU 292	74.484 42.085 28.742 1.00 32.33 74.312 40.967 29.232 1.00 32.22
	ATOM		75.627 42.750 28.846 1.00 30.31
	ATOM	1026 N GLY 293 1027 CA GLY 293	76.751 42.176 29.561 1.00 30.51
25	ATOM	1027 CA GL1 293	77.238 40.894 28.913 1.00 29.87
25	ATOM ATOM	1028 C GL1 293 1029 O GLY 293	77.432 40.843 27.698 1.00 35.43
	ATOM	1030 N VAL 294	77.392 39.848 29.714 1.00 31.88
	ATOM	1030 N VAL 294	77.866 38.561 29.217 1.00 35.77
	ATOM	1031 CA VAL 294	78.232 37.590 30.363 1.00 34.29
30	ATOM	1033 CG1 VAL 294	79.462 38.092 31.095 1.00 37.54
50	ATOM	1034 CG2 VAL 294	77.065 37.425 31.322 1.00 25.62
	ATOM	1035 C VAL 294	76.882 37.879 28.274 1.00 35.89
	ATOM	1036 O VAL 294	77.263 36.960 27.541 1.00 37.99
	ATOM	1037 N VAL 295	75.619 38.304 28.305 1.00 34.41
35	ATOM	1038 CA VAL 295	74.616 37.728 27.413 1.00 32.98
	ATOM	1039 CB VAL 295	73.208 38.298 27.677 1.00 31.25
	ATOM	1040 CG1 VAL 295	72.208 37.706 26.694 1.00 23.54
	ATOM	1041 CG2 VAL 295	72.783 37.993 29.101 1.00 23.07
	ATOM	1042 C VAL 295	75.057 38.062 25.993 1.00 33.92
40	ATOM	1043 O VAL 295	74.932 37.238 25.090 1.00 36.95
	ATOM	1044 N SER 296	75.625 39.253 25.820 1.00 31.27
	ATOM	1045 CA SER 296	76.118 39.695 24.521 1.00 33.38
	ATOM	1046 CB SER 296	76.667 41.115 24.620 1.00 24.78
	ATOM	1047 OG SER 296	77.368 41.478 23.449 1.00 25.43
45	ATOM	1048 C SER 296	77.216 38.748 24.045 1.00 35.86
	ATOM	1049 O SER 296	77.220 38.324 22.886 1.00 39.60
	ATOM	1050 N ASP 297	78.135 38.402 24.943 1.00 37.41
	ATOM	1051 CA ASP 297	79.227 37.490 24.602 1.00 35.39
	ATOM	1052 CB ASP 297	80.147 37.269 25.808 1.00 43.07
50	ATOM	1053 CG ASP 297	80.839 38.540 26.266 1.00 45.07

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81.175 39.398 25.419 1.00 48.02
    ATOM 1054 OD1 ASP 297
    ATOM 1055 OD2 ASP 297
                                81.064 38.670 27.485 1.00 50.13
                               78.662 36.145 24.161 1.00 30.87
    ATOM 1056 C ASP 297
                               79.155 35.534 23.213 1.00 33.92
    ATOM 1057 O ASP 297
                               77.625 35.698 24.861 1.00 28.96
    ATOM 1058 N ALA 298
                                76.971 34.428 24.574 1.00 30.60
    ATOM 1059 CA ALA 298
                                75.889 34.157 25.610 1.00 27.56
    ATOM 1060 CB ALA 298
                               76.377 34.408 23.163 1.00 33.04
    ATOM 1061 C ALA 298
    ATOM 1062 O ALA 298
                               76.538 33.426 22.426 1.00 32.48
    ATOM 1063 N ILE 299
                              75.706 35.493 22.786 1.00 30.92
10
                               75.091 35.588 21.468 1.00 24.71
    ATOM 1064 CA ILE 299
                               74.138 36.789 21.368 1.00 22.98
    ATOM 1065 CB ILE 299
                               73.430 36.786 20.018 1.00 21.90
    ATOM 1066 CG2 ILE 299
    ATOM 1067 CG1 ILE 299
                               73.091 36.707 22.477 1.00 20.91
                               72.266 37.951 22.634 1.00 19.86
    ATOM 1068 CD1 ILE 299
15
                              76.168 35.680 20.395 1.00 26.77
    ATOM 1069 C ILE 299
                              76.036 35.069 19.335 1.00 30.21
    ATOM 1070 O ILE 299
    ATOM 1071 N PHE 300
                               77.238 36.428 20.673 1.00 29.08
                                78.345 36.562 19.726 1.00 28.06
    ATOM 1072 CA PHE 300
     ATOM 1073 CB PHE 300
                                79.386 37.565 20.235 1.00 29.06
20
                                79.289 38.920 19.590 1.00 28.14
    ATOM 1074 CG PHE 300
                                78.449 39.896 20.113 1.00 27.20
    ATOM 1075 CD1 PHE 300
    ATOM 1076 CD2 PHE 300
                                80.017 39.209 18.437 1.00 29.11
                                78.332 41.139 19.499 1.00 28.18
    ATOM 1077 CE1 PHE 300
                                79.908 40.450 17.815 1.00 29.07
    ATOM 1078 CE2 PHE 300
25
                               79.064 41.416 18.348 1.00 22.61
    ATOM 1079 CZ PHE 300
    ATOM 1080 C PHE 300
                               78.991 35.201 19.485 1.00 29.00
                               79.278 34.833 18.344 1.00 30.35
    ATOM 1081 O PHE 300
                               79.183 34.442 20.560 1.00 31.81
     ATOM 1082 N GLU 301
                                79.767 33.111 20.470 1.00 34.96
     ATOM 1083 CA GLU 301
30
                                79.962 32.528 21.865 1.00 30.78
     ATOM 1084 CB GLU 301
                               78.850 32.210 19.634 1.00 35.49
     ATOM 1085 C GLU 301
                               79.322 31.438 18.793 1.00 35.76
     ATOM 1086 O GLU 301
     ATOM 1087 N LEU 302
                               77.543 32.313 19.869 1.00 32.14
                                76.559 31.522 19.132 1.00 25.56
     ATOM 1088 CA LEU 302
35
                                75.147 31.760 19.682 1.00 23.33
     ATOM 1089 CB LEU 302
                                73.992 31.006 19.010 1.00 28.73
     ATOM 1090 CG LEU 302
                                74.093 29.509 19.270 1.00 23.93
     ATOM 1091 CD1 LEU 302
                                72.667 31.551 19.514 1.00 21.32
     ATOM 1092 CD2 LEU 302
                               76,617 31.885 17.650 1.00 23.10
40
     ATOM 1093 C LEU 302
     ATOM 1094 O LEU 302
                               76.664 31.001 16.796 1.00 26.79
                               76.672 33.181 17.353 1.00 22.79
     ATOM 1095 N GLY 303
                                76.745 33.631 15.974 1.00 21.60
     ATOM 1096 CA GLY 303
     ATOM 1097 C GLY 303
                               77.978 33.104 15.256 1.00 30.42
                               77.889 32.619 14.125 1.00 29.18
     ATOM 1098 O GLY 303
45
                               79.132 33.182 15.912 1.00 31.15
     ATOM 1099 N ALA 304
                                80.375 32.703 15.313 1.00 35.44
     ATOM 1100 CA ALA 304
                                81.562 32.995 16.235 1.00 29.16
     ATOM 1101 CB ALA 304
                               80.300 31.208 14.978 1.00 35.15
     ATOM 1102 C ALA 304
                               80.705 30.785 13.891 1.00 37.13
50
     ATOM 1103 O ALA 304
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	ATOM ATOM ATOM ATOM	1104 N SER 305 1105 CA SER 305 1106 CB SER 305 1107 OG SER 305	79.753 30.414 15.892 1.00 33.91 79.638 28.979 15.663 1.00 36.39 79.395 28.237 16.980 1.00 32.71 78.265 28.749 17.663 1.00 48.66
5	ATOM	1108 C SER 305	78.558 28.619 14.641 1.00 37.61
,	ATOM	1109 O SER 305	78.747 27.697 13.845 1.00 39.92
	ATOM	1110 N LEU 306	77.443 29.349 14.651 1.00 38.21
	ATOM	1111 CA LEU 306	76.350 29.092 13.714 1.00 35.65
	ATOM	1112 CB LEU 306	75.094 29.894 14.077 1.00 25.49
10	ATOM	1113 CG LEU 306	74.209 29.374 15.212 1.00 26.18
	ATOM	1114 CD1 LEU 306	72.988 30.262 15.361 1.00 23.40
	ATOM	1115 CD2 LEU 306	73.777 27.952 14.921 1.00 23.57
	ATOM	1116 C LEU 306	76.723 29.356 12.258 1.00 38.05
	ATOM	1117 O LEU 306	76.092 28.809 11.353 1.00 37.22
15	ATOM	1118 N SER 307	77.743 30.185 12.030 1.00 40.41
	ATOM	1119 CA SER 307	78.199 30.511 10.677 1.00 40.85
	ATOM	1120 CB SER 307	79.415 31.442 10.736 1.00 37.32
	ATOM	1121 OG SER 307	79.086 32.678 11.344 1.00 56.20 78.550 29.270 9.852 1.00 39.87
20	ATOM	1122 C SER 307 1123 O SER 307	78.221 29.191 8.670 1.00 44.27
20	ATOM ATOM	1124 N ALA 308	79.207 28.305 10.487 1.00 39.29
	ATOM	1125 CA ALA 308	79.609 27.066 9.826 1.00 33.10
	ATOM	1126 CB ALA 308	80.607 26.310 10.696 1.00 33.37
	ATOM	1127 C ALA 308	78.403 26.177 9.502 1.00 34.07
25	ATOM	1128 O ALA 308	78.467 25.340 8.600 1.00 40.61
	ATOM	1129 N PHE 309	77.305 26.368 10.230 1.00 31.85
	ATOM	1130 CA PHE 309	76.095 25.581 10.015 1.00 35.24
	ATOM	1131 CB PHE 309	75.149 25.698 11.219 1.00 33.69
	ATOM	1132 CG PHE 309	75.618 24.954 12.437 1.00 36.16
30	ATOM	1133 CD1 PHE 309	76.785 25.327 13.090 1.00 43.79
	ATOM	1134 CD2 PHE 309	74.903 23.867 12.922 1.00 38.03
	ATOM	1135 CEI PHE 309	77.237 24.627 14.210 1.00 41.12
	ATOM	1136 CE2 PHE 309	75.346 23.161 14.040 1.00 41.08
2.5	ATOM	1137 CZ PHE 309	76.514 23.543 14.683 1.00 38.37 75.361 25.934 8.720 1.00 36.31
35	ATOM	1138 C PHE 309 1139 O PHE 309	74.633 25.095 8.173 1.00 37.84
	ATOM	1139 O PHE 309 1140 N ASN 310	75.567 27.155 8.225 1.00 35.22
	ATOM ATOM	1141 CA ASN 310	74.933 27.625 6.988 1.00 43.66
	ATOM	1141 CA ASN 310	75.536 26.930 5.760 1.00 54.13
40	ATOM	1142 CB ASN 310	76.980 27.339 5.501 1.00 68.29
70	ATOM	1144 OD1 ASN 310	77.297 28.527 5.412 1.00 74.62
	ATOM	1145 ND2 ASN 310	77.859 26.348 5.352 1.00 68.85
	ATOM	1146 C ASN 310	73.430 27.385 7.013 1.00 38.37
	ATOM	1147 O ASN 310	72.882 26.735 6.123 1.00 36.70
45	ATOM	1148 N LEU 311	72.780 27.865 8.062 1.00 35.22
•	ATOM	1149 CA LEU 311	71.345 27.690 8.206 1.00 34.32
	ATOM	1150 CB LEU 311	70.895 28.054 9.630 1.00 30.19
	ATOM	1151 CG LEU 311	71.458 27.306 10.845 1.00 26.76
	ATOM	1152 CD1 LEU 311	70.792 27.847 12.104 1.00 21.37
50	ATOM	1153 CD2 LEU 311	71.217 25.813 10.722 1.00 22.95

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ATOM 1154 C LEU 311
                               70.601 28.561 7.206 1.00 34.64
                               71.087 29.625 6.820 1.00 37.70
    ATOM 1155 O LEU 311
                              69.444 28.091 6.752 1.00 29.40
    ATOM 1156 N ASP 312
                               68.634 28.867 5.823 1.00 28.65
    ATOM 1157 CA ASP 312
                               68.302 28.061 4.545 1.00 24.79
    ATOM 1158 CB ASP 312
                               67.459 26.804 4.804 1.00 21.47
    ATOM 1159 CG ASP 312
                                66.994 26.549 5.932 1.00 27.92
    ATOM 1160 OD1 ASP 312
                                67.250 26.057 3.832 1.00 27.53
    ATOM 1161 OD2 ASP 312
                              67.380 29.346 6.557 1.00 25.92
    ATOM 1162 C ASP 312
                              67.167 28.985 7.717 1.00 26.98
    ATOM 1163 O ASP 312
10
                              66.540 30.122 5.878 1.00 21.78
    ATOM 1164 N ASP 313
                               65.315 30.653 6.471 1.00 22.89
    ATOM 1165 CA ASP 313
    ATOM 1166 CB ASP 313
                               64.517 31.458 5.439 1.00 29.19
                               65.216 32.739 5.025 1.00 36.82
    ATOM 1167 CG ASP 313
                                65.985 33.285 5.845 1.00 41.51
    ATOM 1168 OD1 ASP 313
15
                                64.997 33.203 3.883 1.00 44.19
    ATOM 1169 OD2 ASP 313
                              64.421 29.587 7.085 1.00 25.09
    ATOM 1170 C ASP 313
                              63.778 29.829 8.110 1.00 27.60
    ATOM 1171 O ASP 313
    ATOM 1172 N THR 314
                               64.363 28.420 6.449 1.00 20.90
                               63.538 27.322 6.942 1.00 22.71
    ATOM 1173 CA THR 314
20
                                63.408 26.208 5.884 1.00 22.07
    ATOM 1174 CB THR 314
    ATOM 1175 OG1 THR 314
                                62.825 26.746 4.693 1.00 23.15
                                62.542 25.079 6.401 1.00 18.17
    ATOM 1176 CG2 THR 314
    ATOM 1177 C THR 314
                               64.080 26.734 8.249 1.00 19.95
                               63.326 26.477 9.182 1.00 22.40
    ATOM 1178 O THR 314
25
                               65.391 26.536 8.318 1.00 20.01
    ATOM 1179 N GLU 315
                                65,997 25,987 9,523 1,00 19,40
    ATOM 1180 CA GLU 315
                                67.454 25.626 9.254 1.00 11.72
    ATOM 1181 CB GLU 315
    ATOM 1182 CG GLU 315
                                67.544 24.440 8.322 1.00 13.43
                                68,925 24.157 7.791 1.00 18.51
    ATOM 1183 CD GLU 315
30
                                69.666 25.107 7.451 1.00 23.24
    ATOM 1184 OE1 GLU 315
                                69.254 22.962 7.673 1.00 24.23
    ATOM 1185 OE2 GLU 315
                               65.833 26.960 10.681 1.00 20.12
    ATOM 1186 C GLU 315
                               65.425 26.570 11.777 1.00 20.53
     ATOM 1187 O GLU 315
                               66.055 28.240 10.406 1.00 21.79
     ATOM 1188 N VAL 316
35
     ATOM 1189 CA VAL 316
                                65.898 29.270 11.425 1.00 18.14
                                66.346 30.659 10.898 1.00 18.97
     ATOM 1190 CB VAL 316
                                66.040 31.741 11.929 1.00 19.08
     ATOM 1191 CG1 VAL 316
                                67.840 30.641 10.537 1.00 17.97
     ATOM 1192 CG2 VAL 316
                               64.430 29.332 11.880 1.00 22.54
40
     ATOM 1193 C VAL 316
                               64.146 29.433 13.072 1.00 26.47
     ATOM 1194 O VAL 316
                               63.505 29.242 10.924 1.00 19.66
     ATOM 1195 N ALA 317
                                62.076 29.286 11.216 1.00 16.99
     ATOM 1196 CA ALA 317
                                61.279 29.329 9.926 1.00 17.79
     ATOM 1197 CB ALA 317
     ATOM 1198 C ALA 317
                               61.619 28.105 12.063 1.00 14.12
45
                               60.808 28.263 12.970 1.00 17.04
     ATOM 1199 O ALA 317
                               62.104 26.911 11.740 1.00 20.37
     ATOM 1200 N LEU 318
                                61.725 25.714 12.485 1.00 21.12
     ATOM 1201 CA LEU 318
                                62.131 24.448 11.718 1.00 21.80
     ATOM 1202 CB LEU 318
     ATOM 1203 CG LEU 318
                                61.364 24.265 10.398 1.00 18.11
50
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	ATOM ATOM ATOM ATOM	1204 CD1 LEU 318 1205 CD2 LEU 318 1206 C LEU 318 1207 O LEU 318	61.946 23.125 9.594 1.00 16.79 59.891 24.024 10.676 1.00 12.66 62.335 25.752 13.880 1.00 22.03 61.688 25.373 14.858 1.00 21.35
5	ATOM ATOM	1208 N LEU 319 1209 CA LEU 319	63.564 26.257 13.964 1.00 20.03 64.260 26.395 15.236 1.00 20.24 65.657 26.960 15.001 1.00 19.07
		1210 CB LEU 319 1211 CG LEU 319 1212 CD1 LEU 319	66.594 27.108 16.196 1.00 27.61 66.518 25.883 17.083 1.00 29.73
10	ATOM ATOM	1213 CD2 LEU 319 1214 C LEU 319	68.012 27.326 15.699 1.00 20.98 63.422 27.334 16.118 1.00 21.16
	ATOM ATOM	1215 O LEU 319 1216 N GLN 320	63.144 27.032 17.279 1.00 26.65 62.958 28.439 15.539 1.00 20.77
15	ATOM ATOM	1217 CA GLN 320 1218 CB GLN 320	62.119 29.390 16.265 1.00 17.87 61.781 30.594 15.388 1.00 18.74
	ATOM ATOM ATOM	1219 CG GLN 320 1220 CD GLN 320 1221 OE1 GLN 320	62.957 31.496 15.111 1.00 21.07 62.637 32.617 14.150 1.00 22.88 61.571 32.653 13.528 1.00 26.07
20	ATOM ATOM	1222 NE2 GLN 320 1223 C GLN 320	63.574 33.537 14.006 1.00 20.11 60.829 28.728 16.730 1.00 19.08
	ATOM ATOM	1224 O GLN 320 1225 N ALA 321	60.368 28.976 17.844 1.00 23.39 60.251 27.886 15.876 1.00 22.71
	ATOM ATOM	1226 CA ALA 321 1227 CB ALA 321	59.010 27.187 16.201 1.00 18.86 58.495 26.422 14.993 1.00 17.22
25	ATOM ATOM ATOM	1228 C ALA 321 1229 O ALA 321 1230 N VAL 322	59.220 26.235 17.376 1.00 19.85 58.362 26.119 18.250 1.00 19.60 60.368 25.561 17.396 1.00 20.25
	ATOM ATOM	1231 CA VAL 322 1232 CB VAL 322	60.693 24.628 18.469 1.00 21.32 61.956 23.800 18.116 1.00 20.46
30	ATOM ATOM	1233 CG1 VAL 322 1234 CG2 VAL 322	62.418 22.971 19.304 1.00 20.39 61.662 22.890 16.930 1.00 16.83
	ATOM ATOM	1235 C VAL 322 1236 O VAL 322	60.880 25.393 19.785 1.00 20.67 60.444 24.941 20.850 1.00 21.28 61.492 26.574 19.701 1.00 21.14
35	ATOM ATOM ATOM	1237 N LEU 323 1238 CA LEU 323 1239 CB LEU 323	61.722 27.417 20.869 1.00 22.94 62.610 28.608 20.511 1.00 16.12
	ATOM ATOM	1240 CG LEU 323 1241 CD1 LEU 323	64.051 28.291 20.115 1.00 22.28 64.719 29.532 19.528 1.00 14.87
40	ATOM ATOM	1242 CD2 LEU 323 1243 C LEU 323	64.816 27.750 21.320 1.00 21.55 60.398 27.932 21.410 1.00 22.55
	ATOM ATOM	1244 O LEU 323 1245 N LEU 324	60.185 27.986 22.615 1.00 25.21 59.507 28.300 20.502 1.00 24.15 58.200 28.827 20.855 1.00 19.88
45	ATOM ATOM ATOM	1246 CA LEU 324 1247 CB LEU 324 1248 CG LEU 324	57.499 29.384 19.608 1.00 15.20 56.067 29.908 19.767 1.00 17.21
.5	ATOM ATOM	1249 CD1 LEU 324 1250 CD2 LEU 324	56.021 31.161 20.637 1.00 15.99 55.496 30.208 18.395 1.00 20.03
	ATOM ATOM	1251 C LEU 324 1252 O LEU 324	57.311 27.795 21.536 1.00 19.83 56.767 28.064 22.609 1.00 24.47
50	ATOM	1253 N MET 325	57.197 26.603 20.956 1.00 25.02

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ATOM 1254 CA MET 325
                                56.339 25.563 21.522 1.00 26.72
                                55.823 24.644 20.410 1.00 30.03
    ATOM 1255 CB MET 325
    ATOM 1256 CG MET 325
                                55.129 25.358 19.241 1.00 25.09
    ATOM 1257 SD MET 325
                               53.714 26.409 19.672 1.00 27.29
                               52.503 25.220 20.084 1.00 20.67
    ATOM 1258 CE MET 325
    ATOM 1259 C MET 325
                               56.995 24.736 22.635 1.00 28.94
    ATOM 1260 O MET 325
                               56.881 23.510 22.672 1.00 32.94
    ATOM 1261 N SER 326
                              57.642 25.418 23.569 1.00 29.36
    ATOM 1262 CA SER 326
                              58.311 24.759 24.680 1.00 31.62
                               59.554 25.559 25.064 1.00 38.13
10
    ATOM 1263 CB SER 326
    ATOM 1264 OG SER 326
                               60.277 24.949 26.119 1.00 48.99
    ATOM 1265 C SER 326
                              57.361 24.653 25.871 1.00 33.69
                              56.620 25.594 26.166 1.00 33.66
    ATOM 1266 O SER 326
                               57.356 23.499 26.536 1.00 38.27
    ATOM 1267 N THR 327
                               56.497 23.306 27.701 1.00 38.98
15
    ATOM 1268 CA THR 327
    ATOM 1269 CB THR 327
                               55.875 21.896 27.730 1.00 33.30
    ATOM 1270 OG1 THR 327
                               56.908 20.911 27.627 1.00 44.01
                                54.888 21.722 26.587 1.00 38.09
    ATOM 1271 CG2 THR 327
    ATOM 1272 C THR 327
                               57.239 23.570 29.018 1.00 42.88
    ATOM 1273 O THR 327
                               56.702 23.325 30.099 1.00 43.36
20
    ATOM 1274 N ASP 328
                              58.462 24.091 28.924 1.00 45.92
    ATOM 1275 CA ASP 328
                               59.268 24.410 30.104 1.00 49.59
                               60.760 24.411 29.760 1.00 59.87
    ATOM 1276 CB ASP 328
                               61.273 23.040 29.387 1.00 75.73
    ATOM 1277 CG ASP 328
25
    ATOM 1278 OD1 ASP 328
                                62.008 22.939 28.382 1.00 85.81
    ATOM 1279 OD2 ASP 328
                                60.946 22.063 30.098 1.00 85.56
    ATOM 1280 C ASP 328
                              58.873 25.767 30.673 1.00 48.50
                              59.725 26.609 30.961 1.00 57.50
    ATOM 1281 O ASP 328
    ATOM 1282 N ARG 329
                               57.569 25.980 30.805 1.00 49.62
                                57.032 27.222 31.340 1.00 50.52
    ATOM 1283 CA ARG 329
30
                               56.400 28.080 30.230 1.00 53.57
    ATOM 1284 CB ARG 329
    ATOM 1285 CG ARG 329
                                57.376 28.828 29.324 1.00 51.09
                                57.897 27.951 28.204 1.00 49.73
    ATOM 1286 CD ARG 329
    ATOM 1287 NE ARG 329
                                58.692 28.699 27.233 1.00 47.44
    ATOM 1288 CZ ARG 329
                                60.005 28.569 27.080 1.00 54.28
35
    ATOM 1289 NH1 ARG 329
                                60.688 27.722 27.839 1.00 58.35
                                60.631 29.256 26.136 1.00 51.92
    ATOM 1290 NH2 ARG 329
                               55.970 26.870 32.375 1.00 51.90
    ATOM 1291 C ARG 329
    ATOM 1292 O ARG 329
                               55.378 25.790 32.324 1.00 50.77
    ATOM 1293 N SER 330
                              55.728 27.784 33.303 1.00 50.56
40
                               54.744 27.564 34.349 1.00 50.67
    ATOM 1294 CA SER 330
    ATOM 1295 CB SER 330
                               55.271 28.108 35.678 1.00 46.64
    ATOM 1296 C SER 330
                              53.404 28.213 34.004 1.00 47.63
    ATOM 1297 O SER 330
                              53.371 29.309 33.440 1.00 48.02
    ATOM 1298 N GLY 331
                               52.314 27.496 34.277 1.00 44.44
45
    ATOM 1299 CA GLY 331
                               50.977 28.023 34.044 1.00 38.77
    ATOM 1300 C GLY 331
                               50.236 27.710 32.756 1.00 41.74
                               49.147 28.246 32.537 1.00 49.57
    ATOM 1301 O GLY 331
                              50.783 26.841 31.912 1.00 39.75
    ATOM 1302 N LEU 332
    ATOM 1303 CA LEU 332
                              50.123 26.502 30.651 1.00 37.55
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51.107 25.829 29.694 1.00 32.36
    ATOM 1304 CB LEU 332
    ATOM 1305 CG LEU 332
                                52.268 26.659 29.153 1.00 34.40
                                53,207 25,749 28,379 1.00 30.22
    ATOM 1306 CD1 LEU 332
    ATOM 1307 CD2 LEU 332
                                51.742 27.786 28.277 1.00 23.33
                               48.921 25.589 30.834 1.00 36.73
    ATOM 1308 C LEU 332
    ATOM 1309 O LEU 332
                               48.987 24.608 31.577 1.00 39.29
    ATOM 1310 N LEU 333
                               47.822 25.925 30.168 1.00 36.07
                                46.615 25.107 30.215 1.00 39.58
    ATOM 1311 CA LEU 333
                                45.384 25.906 29.754 1.00 41.08
    ATOM 1312 CB LEU 333
    ATOM 1313 CG LEU 333
                                44.601 26.883 30.644 1.00 47.59
10
                                44.268 26.213 31.961 1.00 45.65
    ATOM 1314 CD1 LEU 333
                                45.366 28.171 30.874 1.00 47.42
    ATOM 1315 CD2 LEU 333
                               46.791 23.911 29.278 1.00 40.00
    ATOM 1316 C LEU 333
                               46.690 22.754 29.689 1.00 44.77
    ATOM 1317 O LEU 333
                               47.102 24.213 28.022 1.00 37.70
    ATOM 1318 N CYA 334
15
                                47.265 23.209 26.968 1.00 36.04
     ATOM 1319 CA CYA 334
    ATOM 1320 CB CYA 334
                                46.815 23.808 25.635 1.00 40.64
    ATOM 1321 SG CYA 334
                                45,280 24,738 25,758 1.00 44,31
                                43.972 22.946 25.380 1.00 76.30
    ATOM 1322 AS CYA 334
    ATOM 1323 C CYA 334
                               48.668 22.617 26.815 1.00 34.91
20
                               49.237 22.615 25.722 1.00 37.63
     ATOM 1324 O CYA 334
     ATOM 1325 N VAL 335
                               49.189 22.056 27.903 1.00 35.43
     ATOM 1326 CA VAL 335
                                50.518 21.452 27.909 1.00 34.27
                                50.861 20.868 29.298 1.00 34.21
     ATOM 1327 CB VAL 335
                                52.261 20.258 29.292 1.00 33.66
     ATOM 1328 CG1 VAL 335
25
     ATOM 1329 CG2 VAL 335
                                50.755 21.945 30.362 1.00 31.77
     ATOM 1330 C VAL 335
                               50.662 20.349 26.865 1.00 37.14
                               51.639 20.320 26.114 1.00 37.59
     ATOM 1331 O VAL 335
                               49.683 19.451 26.813 1.00 39.99
     ATOM 1332 N ASP 336
                                49.705 18.339 25.866 1.00 41.64
     ATOM 1333 CA ASP 336
30
                                48.532 17.392 26.146 1.00 54.27
     ATOM 1334 CB ASP 336
                                48.596 16.118 25.322 1.00 67.42
     ATOM 1335 CG ASP 336
     ATOM 1336 OD1 ASP 336
                                47.915 16.049 24.274 1.00 70.98
     ATOM 1337 OD2 ASP 336
                                49.337 15.191 25.717 1.00 76.88
                               49.702 18.762 24.393 1.00 38.31
     ATOM 1338 C ASP 336
35
                               50.469 18.229 23.586 1.00 37.46
     ATOM 1339 O ASP 336
                               48.853 19.729 24.052 1.00 30.23
     ATOM 1340 N LYS 337
                                48.740 20.211 22.676 1.00 29.21
     ATOM 1341 CA LYS 337
     ATOM 1342 CB LYS 337
                                47.561 21.189 22.559 1.00 30.53
     ATOM 1343 CG LYS 337
                                47.012 21.360 21.162 1.00 51.63
40
     ATOM 1344 CD LYS 337
                                45.636 21.997 21.186 1.00 59.57
                                45.066 22.115 19.774 1.00 66.05
     ATOM 1345 CE LYS 337
                                43.673 22.693 19.776 1.00 67.20
     ATOM 1346 NZ LYS 337
                               50.054 20.873 22.249 1.00 28.33
     ATOM 1347 C LYS 337
                               50.581 20.594 21.170 1.00 26.08
     ATOM 1348 O. LYS 337
45
                               50.609 21.696 23.141 1.00 26.74
     ATOM 1349 N ILE 338
                               51.873 22.390 22.902 1.00 25.42
     ATOM 1350 CA ILE 338
                               52.177 23.379 24.052 1.00 23.57
     ATOM 1351 CB ILE 338
     ATOM 1352 CG2 ILE 338
                               53.559 23.991 23.874 1.00 22.59
                                51.105 24.471 24.096 1.00 23.57
     ATOM 1353 CG1 ILE 338
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51.157 25.362 25.333 1.00 24.30
    ATOM 1354 CD1 ILE 338
    ATOM 1355 C ILE 338
                              53.018 21.382 22.768 1.00 29.20
    ATOM 1356 O ILE 338
                              53.905 21.537 21.916 1.00 31.59
                               52.977 20.340 23.595 1.00 34.82
    ATOM 1357 N GLU 339
                                53.980 19.277 23.597 1.00 34.23
    ATOM 1358 CA GLU 339
    ATOM 1359 CB GLU 339
                                53.639 18.256 24.681 1.00 40.38
                                54.785 17.354 25.072 1.00 54.98
    ATOM 1360 CG GLU 339
                                55.644 17.964 26.178 1.00 71.26
    ATOM 1361 CD GLU 339
    ATOM 1362 OE1 GLU 339
                                56.766 18.444 25.858 1.00 77.82
                                55.170 17.985 27.349 1.00 65.14
    ATOM 1363 OE2 GLU 339
10
                               53.972 18.582 22.231 1.00 34.42
    ATOM 1364 C GLU 339
                               55.018 18.431 21.590 1.00 29.41
    ATOM 1365 O GLU 339
    ATOM 1366 N LYS 340
                               52.778 18.189 21.786 1.00 34.13
                               52.592 17.513 20.502 1.00 32.05
    ATOM 1367 CA LYS 340
    ATOM 1368 CB LYS 340
                               51.121 17.105 20.325 1.00 34.59
15
                               53.064 18.390 19.337 1.00 32.56
    ATOM 1369 C LYS 340
                               53.762 17.913 18.441 1.00 32.93
    ATOM 1370 O LYS 340
    ATOM 1371 N SER 341
                               52.725 19.677 19.374 1.00 31.42
    ATOM 1372 CA SER 341
                               53.134 20.621 18.334 1.00 27.79
                               52.559 22.009 18.601 1.00 27.85
    ATOM 1373 CB SER 341
20
                               51.149 21.966 18.579 1.00 47.20
    ATOM 1374 OG SER 341
                               54.647 20.713 18.240 1.00 26.01
    ATOM 1375 C SER 341
    ATOM 1376 O SER 341
                               55.205 20.706 17.139 1.00 27.10
                               55.318 20.794 19.389 1.00 24.25
    ATOM 1377 N GLN 342
                                56.771 20.875 19.392 1.00 27.16
    ATOM 1378 CA GLN 342
25
                                57.309 21.089 20.799 1.00 25.60
    ATOM 1379 CB GLN 342
    ATOM 1380 CG GLN 342
                                58.768 21.466 20.777 1.00 27.99
    ATOM 1381 CD GLN 342
                                59.407 21.429 22.133 1.00 29.58
                                60.123 22.356 22.513 1.00 31.18
    ATOM 1382 OE1 GLN 342
                                59.184 20.345 22.868 1.00 29.17
    ATOM 1383 NE2 GLN 342
30
                               57.377 19.609 18.786 1.00 28.45
    ATOM 1384 C GLN 342
    ATOM 1385 O GLN 342
                               58.378 19.675 18.062 1.00 29.79
                               56.777 18.458 19.078 1.00 26.58
    ATOM 1386 N GLU 343
                                57.251 17.190 18.525 1.00 30.07
    ATOM 1387 CA GLU 343
                                56.462 16.016 19.114 1.00 40.79
    ATOM 1388 CB GLU 343
35
                                56.812 15.700 20.568 1.00 61.22
    ATOM 1389 CG GLU 343
                                55.951 14.594 21.166 1.00 71.76
    ATOM 1390 CD GLU 343
    ATOM 1391 OE1 GLU 343
                                55.472 13.719 20.405 1.00 76.73
                                55.758 14.601 22.403 1.00 74.09
    ATOM 1392 OE2 GLU 343
                               57.097 17.225 17.001 1.00 25.87
40
    ATOM 1393 C GLU 343
    ATOM 1394 O GLU 343
                               58.008 16.842 16.260 1.00 27.26
                               55.947 17.727 16.550 1.00 23.70
    ATOM 1395 N ALA 344
                                55.647 17.853 15.124 1.00 22.16
    ATOM 1396 CA ALA 344
    ATOM 1397 CB ALA 344
                                54.275 18.489 14.927 1.00 21.18
    ATOM 1398 C ALA 344
                               56.729 18.694 14.454 1.00 21.24
45
                               57.303 18.284 13.438 1.00 26.47
    ATOM 1399 O ALA 344
                               57.048 19.840 15.055 1.00 22.48
    ATOM 1400 N TYR 345
    ATOM 1401 CA TYR 345
                                58.073 20.738 14.531 1.00 21.41
                                58.085 22.059 15.304 1.00 20.10
     ATOM 1402 CB TYR 345
                                57.023 23.015 14.830 1.00 15.87
     ATOM 1403 CG TYR 345
50
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ATOM 1405 CE1 TYR 345 54.983 24.259 15.225 1.00 17 ATOM 1406 CD2 TYR 345 57.003 23.448 13.505 1.00 16 ATOM 1407 CE2 TYR 345 55.991 24.269 13.036 1.00 16 5 ATOM 1408 CZ TYR 345 54.984 24.668 13.896 1.00 17.	.86
ATOM 1407 CE2 TYR 345 55.991 24.269 13.036 1.00 16 5 ATOM 1408 CZ TYR 345 54.984 24.668 13.896 1.00 17.	.80
5 ATOM 1408 CZ TYR 345 54.984 24.668 13.896 1.00 17.	
	.84 07
	9/
ATOM 1409 OH TYR 345 53.963 25.455 13.406 1.00 27	11
ATOM 1410 C TYR 345 59.465 20.120 14.548 1.00 24.4	3
ATOM 1411 O TYR 345 60.238 20.291 13.597 1.00 24.6	
ATOM 1412 N LEU 346 59.777 19.401 15.621 1.00 26.7	
10 ATOM 1413 CA LEU 346 61.074 18.746 15.767 1.00 25.	06
ATOM 1414 CB LEU 346 61.207 18.108 17.150 1.00 24.	
ATOM 1415 CG LEU 346 61.637 19.076 18.252 1.00 26.	
ATOM 1416 CD1 LEU 346 61.387 18.468 19.610 1.00 26	
ATOM 1417 CD2 LEU 346 63.101 19.437 18.076 1.00 21	
15 ATOM 1418 C LEU 346 61.322 17.713 14.683 1.00 23.2	4
ATOM 1419 O LEU 346 62.416 17.645 14.127 1.00 27.5	4
ATOM 1420 N LEU 347 60.314 16.900 14.395 1.00 25.3	'5
ATOM 1421 CA-LEU 347 60.437 15.881 13.356 1.00 25	41
ATOM 1422 CB LEU 347 59.208 14.970 13.330 1.00 23.	
20 ATOM 1423 CG LEU 347 59.302 13.713 14.190 1.00 31	85
ATOM 1424 CD1 LEU 347 58.004 12.928 14.089 1.00 39	
ATOM 1425 CD2 LEU 347 60.483 12.864 13.738 1.00 27	
ATOM 1426 C LEU 347 60.611 16.535 11.998 1.00 23.2	
ATOM 1427 O LEU 347 61.468 16.133 11.211 1.00 28.5	
25 ATOM 1428 N ALA 348 59.784 17.542 11.731 1.00 26.	10
ATOM 1429 CA ALA 348 59.840 18.273 10.474 1.00 23	
ATOM 1430 CB ALA 348 58.732 19.324 10.433 1.00 25	
ATOM 1431 C ALA 348 61.210 18.924 10.337 1.00 23.	
ATOM 1432 O ALA 348 61.847 18.835 9.288 1.00 29.1	
30 ATOM 1433 N PHE 349 61.678 19.506 11.438 1.00 24.	
ATOM 1434 CA PHE 349 62.973 20.181 11.493 1.00 20	
ATOM 1435 CB PHE 349 63.164 20.772 12.900 1.00 17	
ATOM 1436 CG PHE 349 64.334 21.721 13.031 1.00 14	
ATOM 1437 CD1 PHE 349 65.109 22.069 11.933 1.00 1	
35 ATOM 1438 CD2 PHE 349 64.651 22.269 14.271 1.00 24	
ATOM 1439 CE1 PHE 349 66.185 22.944 12.063 1.00 20	
ATOM 1440 CE2 PHE 349 65.727 23.147 14.413 1.00 23	
ATOM 1441 CZ PHE 349 66.494 23.486 13.299 1.00 20	
ATOM 1442 C PHE 349 64.084 19.181 11.159 1.00 23.	
40 ATOM 1443 O PHE 349 64.916 19.427 10.278 1.00 24.	
ATOM 1444 N GLU 350 64.057 18.028 11.820 1.00 25.	
ATOM 1445 CA GLU 350 65.060 16.991 11.606 1.00 20	
ATOM 1446 CB GLU 350 64.813 15.822 12.567 1.00 29	.56
ATOM 1447 CG GLU 350 65.774 14.661 12.391 1.00 39	
45 ATOM 1448 CD GLU 350 65.574 13.549 13.407 1.00 45	.06
ATOM 1449 OE1 GLU 350 64.413 13.192 13.715 1.00 4	9.26
ATOM 1450 OE2 GLU 350 66.593 13.017 13.887 1.00 5	
ATOM 1451 C GLU 350 65.051 16.494 10.162 1.00 26	
ATOM 1452 O GLU 350 66.096 16.398 9.513 1.00 28.	77
50 ATOM 1453 N HIS 351 63.858 16.219 9.652 1.00 22.5	5

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ATOM 1454 CA HIS 351
                               63.699 15.728 8.294 1.00 22.20
                              62.263 15.265 8.083 1.00 22.47
    ATOM 1455 CB HIS 351
                               61.881 14.106 8.947 1.00 23.61
    ATOM 1456 CG HIS 351
                               62.633 13.300 9.739 1.00 27.65
    ATOM 1457 CD2 HIS 351
                               60.585 13.653 9.069 1.00 26.13
    ATOM 1458 ND1 HIS 351
                               60.548 12.629 9.898 1.00 22.87
    ATOM 1459 CE1 HIS 351
                               61.779 12.393 10.319 1.00 27.53
    ATOM 1460 NE2 HIS 351
                              64.135 16.764 7.259 1.00 21.76
    ATOM 1461 C HIS 351
                              64.708 16.419 6.226 1.00 27.02
    ATOM 1462 O HIS 351
                               63.909 18.041 7.555 1.00 18.26
    ATOM 1463 N TYR 352
10
    ATOM 1464 CA TYR 352
                               64.327 19.101 6.649 1.00 16.94
                               63.749 20.455 7.066 1.00 19.07
    ATOM 1465 CB TYR 352
                               64.107 21.534 6.081 1.00 21.11
    ATOM 1466 CG TYR 352
                                63.518 21.564 4.819 1.00 21.33
    ATOM 1467 CD1 TYR 352
                                63.921 22.482 3.859 1.00 21.06
15
    ATOM 1468 CE1 TYR 352
                                65.105 22.462 6.367 1.00 22.07
    ATOM 1469 CD2 TYR 352
    ATOM 1470 CE2 TYR 352
                                65.515 23.388 5.412 1.00 25.40
                               64.921 23.384 4.161 1.00 21.90
    ATOM 1471 CZ TYR 352
                               65.334 24.268 3.197 1.00 23.57
    ATOM 1472 OH TYR 352
                               65.853 19.156 6.657 1.00 18.49
    ATOM 1473 C TYR 352
20
    ATOM 1474 O TYR 352
                               66.487 19.323 5.609 1.00 24.99
                               66.451 19.008 7.836 1.00 24.64
    ATOM 1475 N VAL 353
                               67.904 19.011 7.955 1.00 22.20
    ATOM 1476 CA VAL 353
                               68.350 18.925 9.440 1.00 23.72
    ATOM 1477 CB VAL 353
                                69.838 18.597 9.546 1.00 21.24
    ATOM 1478 CG1 VAL 353
25
    ATOM 1479 CG2 VAL 353
                                68.063 20.245 10.142 1.00 20.07
                               68.452 17.829 7.146 1.00 25.07
    ATOM 1480 C VAL 353
                               69.467 17.955 6.457 1.00 24.75
    ATOM 1481 O VAL 353
                               67.768 16.690 7.221 1.00 24.59
    ATOM 1482 N ASN 354
                               68.171 15.502 6.474 1.00 25.64
    ATOM 1483 CA ASN 354
30
                               67.223 14.331 6.751 1.00 26.05
    ATOM 1484 CB ASN 354
                                67.368 13.763 8.151 1.00 30.27
    ATOM 1485 CG ASN 354
                                66.443 13.139 8.672 1.00 33.71
    ATOM 1486 OD1 ASN 354
                                68.529 13.959 8.765 1.00 34.78
    ATOM 1487 ND2 ASN 354
                               68.143 15.813 4.981 1.00 30.50
    ATOM 1488 C ASN 354
35
                               69.042 15.423 4.233 1.00 33.73
    ATOM 1489 O ASN 354
    ATOM 1490 N HIS 355
                              67.098 16.519 4.555 1.00 30.54
                               66.926 16.901 3.157 1.00 26.02
    ATOM 1491 CA HIS 355
                               65.535 17.521 2.953 1.00 29.93
    ATOM 1492 CB HIS 355
                               65.367 18.217 1.638 1.00 37.91
     ATOM 1493 CG HIS 355
40
                               65.654 19.486 1.264 1.00 31.26
     ATOM 1494 CD2 HIS 355
                               64.861 17.593 0.518 1.00 32.67
     ATOM 1495 ND1 HIS 355
                               64.843 18.447 -0.488 1.00 33.22
     ATOM 1496 CE1 HIS 355
                               65,322 19.601 -0.061 1.00 32.69
     ATOM 1497 NE2 HIS 355
                              68.009 17.851 2.652 1.00 24.29
     ATOM 1498 C HIS 355
45
                              68.381 17.798 1.484 1.00 26.82
     ATOM 1499 O HIS 355
                               68.484 18.735 3.526 1.00 29.72
     ATOM 1500 N ARG 356
                                69.516 19.711 3.167 1.00 26.65
     ATOM 1501 CA ARG 356
                                69.593 20.804 4.225 1.00 22.74
     ATOM 1502 CB ARG 356
                                68.409 21.735 4.222 1.00 21.64
     ATOM 1503 CG ARG 356
50
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68.757 23.024 3.524 1.00 28.04
    ATOM 1504 CD ARG 356
    ATOM 1505 NE ARG 356
                                69.550 23.900 4.380 1.00 33.79
                                70.508 24.716 3.952 1.00 29.26
    ATOM 1506 CZ ARG 356
                                70.814 24,776 2.667 1.00 29.08
    ATOM 1507 NH1 ARG 356
                                71.136 25.493 4.816 1.00 33.61
    ATOM 1508 NH2 ARG 356
                               70.904 19.115 2.950 1.00 27.58
    ATOM 1509 C ARG 356
    ATOM 1510 O ARG 356
                               71.757 19.740 2.312 1.00 31.44
                               71.140 17.937 3.519 1.00 30.56
    ATOM 1511 N LYS 357
    ATOM 1512 CA LYS 357
                               72.422 17.244 3.390 1.00 34.56
                               72.500 16.518 2.043 1.00 39.66
    ATOM 1513 CB LYS 357
10
                               71.476 15.402 1.871 1.00 42.16
    ATOM 1514 CG LYS 357
    ATOM 1515 CD LYS 357
                               71.674 14.676 0.550 1.00 54.23
                               70.691 13.523 0.371 1.00 61.97
    ATOM 1516 CE LYS 357
                               69.288 13.974 0.162 1.00 65.88
    ATOM 1517 NZ LYS 357
                               73.665 18.119 3.606 1.00 36.73
    ATOM 1518 C LYS 357
15
    ATOM 1519 O LYS 357
                              74.522 18.248 2.728 1.00 40.70
    ATOM 1520 N HIS 358
                              73.738 18.732 4.786 1.00 33.69
                               74.863 19.581 5.163 1.00 33.59
    ATOM 1521 CA HIS 358
                               74.660 20.155 6.571 1.00 32.07
    ATOM 1522 CB HIS 358
    ATOM 1523 CG HIS 358
                               73.593 21.200 6.666 1.00 29.74
20
                               72.245 21.098 6.736 1.00 23.35
    ATOM 1524 CD2 HIS 358
    ATOM 1525 ND1 HIS 358
                               73.876 22.547 6.731 1.00 28.13
                               72.752 23.231 6.834 1.00 26.94
    ATOM 1526 CE1 HIS 358
                               71.747 22.373 6.838 1.00 23.32
    ATOM 1527 NE2 HIS 358
                              76.121 18.720 5.180 1.00 37.98
25
    ATOM 1528 C HIS 358
    ATOM 1529 O HIS 358
                              76.087 17.581 5.654 1.00 41.07
                               77.231 19.261 4.690 1.00 44.20
    ATOM 1530 N ASN 359
                               78.492 18.523 4.676 1.00 49.72
    ATOM 1531 CA ASN 359
                               79,406 19.053 3.572 1.00 46.66
    ATOM 1532 CB ASN 359
     ATOM 1533 C ASN 359
                               79.174 18.648 6.039 1.00 51.77
30
     ATOM 1534 O ASN 359
                               80.356 18.985 6.122 1.00 57.32
                              78.414 18.383 7.101 1.00 51.04
     ATOM 1535 N ILE 360
                               78.906 18.471 8.477 1.00 48.24
     ATOM 1536 CA ILE 360
                               78,340 19.721 9.207 1.00 47.20
     ATOM 1537 CB ILE 360
                               78.781 19.741 10.673 1.00 43.50
    ATOM 1538 CG2 ILE 360
35
                               78.777 21.005 8.491 1.00 45.94
     ATOM 1539 CG1 ILE 360
     ATOM 1540 CD1 ILE 360
                               78.157 22.262 9.050 1.00 43.00
     ATOM 1541 C ILE 360
                              78,462 17.222 9.239 1.00 47.23
                              77.272 16.901 9.278 1.00 45.13
     ATOM 1542 O ILE 360
     ATOM 1543 N PRO 361
                               79.416 16.490 9.838 1.00 48.61
40
                                80.869 16.705 9.729 1.00 50.93
     ATOM 1544 CD PRO 361
     ATOM 1545 CA PRO 361
                                79.129 15.270 10.599 1.00 45.46
     ATOM 1546 CB PRO 361
                                80.524 14.725 10.927 1.00 49.01
                                81,402 15.307 9.862 1.00 54.41
     ATOM 1547 CG PRO 361
                               78.330 15.514 11.879 1.00 36.54
     ATOM 1548 C PRO 361
45
                               78.666 16.394 12.672 1.00 39.83
     ATOM 1549 O PRO 361
     ATOM 1550 N HIS 362
                              77.282 14.716 12.075 1.00 31.35
                               76.430 14.798 13.264 1.00 33.34
     ATOM 1551 CA HIS 362
                               77.246 14.495 14.524 1.00 33.77
     ATOM 1552 CB HIS 362
                               78.129 13.292 14.397 1.00 34.40
     ATOM 1553 CG HIS 362
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77.837 11.999 14.130 1.00 32.60
     ATOM 1554 CD2 HIS 362
                                79.501 13.362 14.506 1.00 36.14
     ATOM 1555 ND1 HIS 362
                                80.017 12.160 14.311 1.00 36.26
     ATOM 1556 CE1 HIS 362
                                79.029 11.316 14.080 1.00 35.73
     ATOM 1557 NE2 HIS 362
                              75.778 16.164 13.389 1.00 33.55
    ATOM 1558 C HIS 362
     ATOM 1559 O HIS 362
                               75.539 16.652 14.495 1.00 31.93
                               75.449 16.748 12.240 1.00 35.83
    ATOM 1560 N PHE 363
                                74.834 18.067 12.166 1.00 30.93
     ATOM 1561 CA PHE 363
     ATOM 1562 CB PHE 363
                                74.464 18.394 10.712 1.00 28.82
                                73.959 19.797 10.514 1.00 26.59
     ATOM 1563 CG PHE 363
10
                                74.846 20.843 10.301 1.00 26.96
     ATOM 1564 CD1 PHE 363
                                72.596 20.076 10.575 1.00 27.51
     ATOM 1565 CD2 PHE 363
                                74.384 22.151 10.155 1.00 31.83
     ATOM 1566 CE1 PHE 363
                                72.124 21.378 10.433 1.00 26.65
     ATOM 1567 CE2 PHE 363
                                73.019 22.417 10.223 1.00 24.42
     ATOM 1568 CZ PHE 363
15
                               73.613 18.235 13.063 1.00 28.73
     ATOM 1569 C PHE 363
    ATOM 1570 O PHE 363
                               73.550 19.174 13.848 1.00 25.33
                               72.663 17.310 12.969 1.00 22.89
     ATOM 1571 N TRP 364
                                71.443 17.405 13.760 1.00 24.19
     ATOM 1572 CA TRP 364
                                70.481 16.254 13.439 1.00 26.31
     ATOM 1573 CB TRP 364
20
                                69.198 16.275 14.228 1.00 20.24
     ATOM 1574 CG TRP 364
     ATOM 1575 CD2 TRP 364
                                68.213 17.325 14.262 1.00 24.50
                                67.175 16.894 15.120 1.00 25.84
     ATOM 1576 CE2 TRP 364
                                68.106 18.583 13.652 1.00 25.83
     ATOM 1577 CE3 TRP 364
                                68.731 15.289 15.040 1.00 23.61
     ATOM 1578 CD1 TRP 364
25
     ATOM 1579 NE1 TRP 364
                                67.515 15.648 15.579 1.00 32.26
                                66.048 17.674 15.386 1.00 21.95
     ATOM 1580 CZ2 TRP 364
                                66.979 19.360 13.919 1.00 20.73
     ATOM 1581 CZ3 TRP 364
                                65.967 18.899 14.779 1.00 22.37
     ATOM 1582 CH2 TRP 364
     ATOM 1583 C TRP 364
                               71.663 17.551 15.267 1.00 28.84
30
                               71.246 18.554 15.839 1.00 31.25
     ATOM 1584 O TRP 364
     ATOM 1585 N PRO 365
                               72.305 16.568 15.932 1.00 29.69
                                72,790 15.245 15.497 1.00 30.89
     ATOM 1586 CD PRO 365
                                72.499 16.748 17.373 1.00 25.62
     ATOM 1587 CA PRO 365
                                73.195 15.451 17.810 1.00 25.50
     ATOM 1588 CB PRO 365
35
                                73.804 14.915 16.560 1.00 34.15
     ATOM 1589 CG PRO 365
                               73.320 18.002 17.698 1.00 24.07
     ATOM 1590 C PRO 365
                               73.079 18.654 18.711 1.00 23.58
     ATOM 1591 O PRO 365
                               74.250 18.365 16.820 1.00 24.09
     ATOM 1592 N LYS 366
     ATOM 1593 CA LYS 366
                                75.063 19.562 17.027 1.00 29.44
40
                                76.131 19.681 15.945 1.00 27.18
     ATOM 1594 CB LYS 366
                                77.341 18.802 16.149 1.00 23.71
     ATOM 1595 CG LYS 366
                                78.304 19.019 15.001 1.00 27.50
     ATOM 1596 CD LYS 366
                                79.624 18.329 15.231 1.00 35.88
     ATOM 1597 CE LYS 366
                                80.550 18.591 14.097 1.00 41.92
45
     ATOM 1598 NZ LYS 366
                               74.195 20.820 17.012 1.00 32.76
     ATOM 1599 C LYS 366
     ATOM 1600 O LYS 366
                               74.326 21.694 17.873 1.00 36.13
     ATOM 1601 N LEU 367
                               73.307 20.907 16.028 1.00 33.70
                                72.409 22.041 15.905 1.00 30.60
     ATOM 1602 CA LEU 367
     ATOM 1603 CB LEU 367
                                71.636 21.955 14.587 1.00 24.26
50
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	ATOM	1604 CG LEU 367	70.675 23.103 14.274 1.00 32.42
	ATOM	1605 CD1 LEU 367	71.394 24.440 14.404 1.00 24.78
	ATOM	1606 CD2 LEU 367	70.098 22.924 12.878 1.00 28.84
	ATOM	1607 C LEU 367	71.450 22.015 17.087 1.00 31.90
5	ATOM	1608 O LEU 367	71.113 23.052 17.655 1.00 39.20
	ATOM	1609 N LEU 368	71.051 20.812 17.485 1.00 33.86
	ATOM	1610 CA LEU 368	70.144 20.617 18.608 1.00 32.97
	ATOM	1611 CB LEU 368	69.866 19.123 18.759 1.00 34.22
	ATOM	1612 CG LEU 368	68.458 18.633 19.084 1.00 38.15
10	ATOM	1613 CD1 LEU 368	67.400 19.449 18.345 1.00 27.75
	ATOM	1614 CD2 LEU 368	68.374 17.154 18.733 1.00 31.51
	ATOM	1615 C LEU 368	70.793 21.181 19.875 1.00 35.29
	ATOM	1616 O LEU 368	70.128 21.806 20.703 1.00 36.16
	ATOM	1617 N MET 369	72.106 21.001 19.994 1.00 41.13
15	ATOM	1618 CA MET 369	72.857 21.504 21.139 1.00 40.92
	ATOM	1619 CB MET 369	74.283 20.955 21.115 1.00 43.32
	ATOM	1620 CG MET 369	74.383 19.497 21.545 1.00 50.01
	ATOM	1621 SD MET 369	75.997 18.770 21.190 1.00 56.63
	ATOM	1622 CE MET 369	77.032 19.596 22.409 1.00 62.26
20	ATOM	1623 C MET 369	72.872 23.032 21.186 1.00 43.46
	ATOM	1624 O MET 369	73.137 23.619 22.233 1.00 47.51
	ATOM	1625 N LYS 370	72.594 23.673 20.053 1.00 41.60
	ATOM	1626 CA LYS 370	72.561 25.131 19.988 1.00 34.48
	ATOM	1627 CB LYS 370	72.689 25.623 18.546 1.00 31.53
25	ATOM	1628 CG LYS 370	74.012 25.278 17.896 1.00 30.76
	ATOM	1629 CD LYS 370	75.168 25.774 18.731 1.00 32.16
,	ATOM	1630 CE LYS 370	76.488 25.388 18.116 1.00 31.08
,	ATOM	1631 NZ LYS 370	77.604 25.822 18.993 1.00 51.52
	ATOM	1632 C LYS 370	71.269 25.652 20.606 1.00 36.35
30	ATOM	1633 O LYS 370	71.197 26.806 21.032 1.00 39.02
	ATOM	1634 N VAL 371	70.248 24.804 20.652 1.00 34.33
	ATOM	1635 CA VAL 371	68.975 25.186 21.249 1.00 36.27
	ATOM	1636 CB VAL 371	67.885 24.097 21.046 1.00 36.15
	ATOM	1637 CG1 VAL 371	66.600 24.487 21.758 1.00 32.69
35	ATOM	1638 CG2 VAL 371	67.612 23.892 19.567 1.00 33.75
	ATOM	1639 C VAL 371	69.196 25.423 22.745 1.00 41.55
	ATOM	1640 O VAL 371	68.638 26.367 23.316 1.00 40.82
	ATOM	1641 N THR 372	70.018 24.581 23.378 1.00 40.42
	ATOM	1642 CA THR 372	70.300 24.733 24.804 1.00 41.69
40	ATOM	1643 CB THR 372	71.037 23.499 25.397 1.00 42.36
	ATOM	1644 OG1 THR 372	72.125 23.133 24.548 1.00 53.57
	ATOM	1645 CG2 THR 372	70.090 22.313 25.523 1.00 43.54
	ATOM	1646 C THR 372	71.090 26.021 25.048 1.00 38.75
	ATOM	1647 O THR 372	70.858 26.714 26.042 1.00 37.51
45	ATOM	1648 N ASP 373	71.987 26.360 24.122 1.00 36.73
	ATOM	1649 CA ASP 373	72.768 27.594 24.223 1.00 30.96
	ATOM	1650 CB ASP 373	73.741 27.732 23.047 1.00 31.26
	ATOM	1651 CG ASP 373	74.865 26.707 23.085 1.00 35.85
	ATOM	1652 OD1 ASP 373	75.523 26.508 22.042 1.00 36.73
50	ATOM	1653 OD2 ASP 373	75.102 26.103 24.153 1.00 39.92

		1654 C 4CD 250	71 707 00 740 04 000 1 00 31 30
	ATOM	1654 C ASP 373	71.797 28.769 24.230 1.00 31.30
	ATOM	1655 O ASP 373	71.926 29.689 25.039 1.00 35.37
	ATOM	1656 N LEU 374	70.804 28.711 23.348 1.00 27.72
_	ATOM	1657 CA LEU 374	69.783 29.751 23.257 1.00 28.18
5	ATOM	1658 CB LEU 374	68.881 29.521 22.042 1.00 28.41
	ATOM	1659 CG LEU 374	69.391 30.055 20.703 1.00 29.87
	ATOM	1660 CD1 LEU 374	68.533 29.520 19.563 1.00 25.44
	ATOM	1661 CD2 LEU 374	69.385 31.581 20.728 1.00 23.74
	ATOM	1662 C LEU 374	68.946 29.786 24.527 1.00 28.61
10	ATOM	1663 O LEU 374	68.516 30.859 24.968 1.00 29.51
	ATOM	1664 N ARG 375	68.690 28.615 25.105 1.00 32.32
	ATOM	1665 CA ARG 375	67.925 28.532 26.345 1.00 33.19
	ATOM	1666 CB ARG 375	67.758 27.074 26.776 1.00 41.70
	ATOM	1667 CG ARG 375	66.360 26.524 26.609 1.00 51.03
15	ATOM	1668 CD ARG 375	65.979 26.416 25.153 1.00 60.16
	ATOM	1669 NE ARG 375	64.648 25.840 24.987 1.00 74.28
	ATOM	1670 CZ ARG 375	64.324 24.587 25.296 1.00 79.34
	ATOM	1671 NH1 ARG 375	
	ATOM	1672 NH2 ARG 375	•
20	ATOM	1673 C ARG 375	68.692 29.296 27.423 1.00 32.02
	ATOM	1674 O ARG 375	68.132 30.150 28.108 1.00 30.42
	ATOM	1675 N MET 376	69.993 29.020 27.521 1.00 32.30
	ATOM	1676 CA MET 376	70.860 29.668 28.499 1.00 36.82
	ATOM	1677 CB MET 376	72.278 29.097 28.433 1.00 45.36
25	ATOM	1678 CG MET 376	72.375 27.645 28.866 1.00 66.71
	ATOM	1679 SD MET 376	74.078 27.057 28.966 1.00 89.64
	ATOM	1680 CE MET 376	74.256 26.229 27.400 1.00 85.51
	ATOM	1681 C MET 376	70.880 31.182 28.310 1.00 37.49
	ATOM	1682 O MET 376	70.780 31.928 29.281 1.00 39.99
30	ATOM	1683 N ILE 377	71.008 31.630 27.060 1.00 33.14
	ATOM	1684 CA ILE 377	71.009 33.057 26.740 1.00 25.98
	ATOM	1685 CB ILE 377	71.181 33.291 25.211 1.00 22.79
	ATOM	1686 CG2 ILE 377	70.838 34.727 24.834 1.00 25.29
	ATOM	1687 CG1 ILE 377	72.606 32.947 24.785 1.00 21.42
35	ATOM	1688 CD1 ILE 377	72.816 32.971 23.282 1.00 19.37
	ATOM	1689 C ILE 377	69.690 33.664 27.228 1.00 27.11
	ATOM	1690 O ILE 377	69.676 34.727 27.856 1.00 28.09
	ATOM	1691 N GLY 378	68.584 32.969 26.975 1.00 29.34
	ATOM	1692 CA GLY 378	67.292 33.457 27.418 1.00 30.41
40	ATOM	1693 C GLY 378	67.233 33.532 28.934 1.00 36.85
	ATOM	1694 O GLY 378	66.672 34.481 29.489 1.00 36.44
	ATOM	1695 N ALA 379	67.837 32.547 29.603 1.00 37.98
	ATOM	1696 CA ALA 379	67.869 32.483 31.066 1.00 36.44
	ATOM	1697 CB ALA 379	68.415 31.133 31.528 1.00 35.63
45	ATOM	1698 C ALA 379	68.712 33.613 31.642 1.00 34.14
	ATOM	1699 O ALA 379	68.259 34.343 32.523 1.00 35.15
	ATOM	1700 N CYA 380	69.941 33.747 31.144 1.00 36.66
	ATOM	1700 K CYA 380	70.860 34.795 31.587 1.00 37.27
	ATOM	1701 CR CYA 380	72.172 34.728 30.810 1.00 36.85
50	ATOM	1702 CB CTA 380	73.201 33.338 31.250 1.00 52.80
20	111011	1705 55 CIA 380	, 5,201 55,550 51,250 1,00 52,00

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ATOM 1704 AS CYA 380
                                74.942 33.593 29.823 1.00 65.79
                               70.230 36.165 31.398 1.00 38.70
    ATOM 1705 C CYA 380
    ATOM 1706 O CYA 380
                               70.337 37.033 32.270 1.00 45.73
                              69.555 36.354 30.265 1.00 37.32
    ATOM 1707 N HIS 381
                               68.906 37.623 29.994 1.00 32.11
    ATOM 1708 CA HIS 381
                               68.377 37.687 28.565 1.00 25.76
    ATOM 1709 CB HIS 381
                               67.596 38.932 28.285 1.00 20.30
    ATOM 1710 CG HIS 381
                               67.998 40.200 28.044 1.00 16.31
    ATOM 1711 CD2 HIS 381
                                66.218 38.971 28.336 1.00 22.06
    ATOM 1712 ND1 HIS 381
                               65.807 40.210 28.146 1.00 21.20
10
    ATOM 1713 CE1 HIS 381
                               66.869 40.976 27.968 1.00 22.58
    ATOM 1714 NE2 HIS 381
                              67.773 37.893 30.980 1.00 32.68
    ATOM 1715 C HIS 381
                              67.602 39.024 31.431 1.00 33.38
    ATOM 1716 O HIS 381
                               66.982 36.873 31.296 1.00 31.27
    ATOM 1717 N ALA 382
                               65.884 37.045 32.243 1.00 29.39
15
    ATOM 1718 CA ALA 382
                                65.121 35.742 32.409 1.00 25.18
    ATOM 1719 CB ALA 382
                               66.420 37.531 33.596 1.00 34.32
    ATOM 1720 C ALA 382
                               65.902 38.501 34.160 1.00 37.79
    ATOM 1721 O ALA 382
                               67.483 36.893 34.085 1.00 36.88
    ATOM 1722 N SER 383
                                68.100 37.268 35.361 1.00 39.74
    ATOM 1723 CA SER 383
20
                                69.233 36.297 35.719 1.00 42.58
    ATOM 1724 CB SER 383
                                68.734 35.010 36.049 1.00 61.85
    ATOM 1725 OG SER 383
                               68.638 38.697 35.311 1.00 36.49
    ATOM 1726 C SER 383
                               68.443 39.480 36.243 1.00 43.81
    ATOM 1727 O SER 383
                               69.305 39.036 34.213 1.00 33.66
    ATOM 1728 N ARG 384
25
    ATOM 1729 CA ARG 384
                                69.866 40.367 34.043 1.00 35.39
                                70.800 40.404 32.835 1.00 29.29
    ATOM 1730 CB ARG 384
                                71.590 41.679 32.731 1.00 29.20
    ATOM 1731 CG ARG 384
                                72.881 41.435 31.995 1.00 37.73
    ATOM 1732 CD ARG 384
                                73.657 42.663 31.850 1.00 48.97
    ATOM 1733 NE ARG 384
30
    ATOM 1734 CZ ARG 384
                                74.346 43.245 32.826 1.00 45.41
                                 74.371 42.715 34.038 1.00 44.51
    ATOM 1735 NH1 ARG 384
                                 75.008 44.368 32.584 1.00 41.43
    ATOM 1736 NH2 ARG 384
                               68,777 41,431 33,916 1.00 39,45
    ATOM 1737 C ARG 384
                                68.913 42.537 34.444 1.00 44.47
    ATOM 1738 O ARG 384
35
                               67.673 41.077 33.270 1.00 36.42
    ATOM 1739 N PHE 385
                                66,568 42.007 33.099 1.00 34.68
    ATOM 1740 CA PHE 385
                                65.444 41.393 32.262 1.00 30.21
    ATOM 1741 CB PHE 385
                                64.263 42.304 32.081 1.00 29.48
    ATOM 1742 CG PHE 385
                                64.289 43.313 31.127 1.00 29.70
    ATOM 1743 CD1 PHE 385
40
                                63.130 42.161 32.873 1.00 28.04
    ATOM 1744 CD2 PHE 385
                                63.203 44.169 30.966 1.00 33.50
    ATOM 1745 CE1 PHE 385
                                62.040 43.012 32.718 1.00 31.35
     ATOM 1746 CE2 PHE 385
                                62.077 44.017 31.763 1.00 32.08
     ATOM 1747 CZ PHE 385
                               66.040 42.412 34.468 1.00 35.76
     ATOM 1748 C PHE 385
                               65.761 43.590 34.693 1.00 40.58
     ATOM 1749 O PHE 385
                               65.906 41.441 35.373 1.00 37.55
     ATOM 1750 N LEU 386
                                65.429 41.706 36.735 1.00 41.01
     ATOM 1751 CA LEU 386
                                65.394 40.413 37.563 1.00 42.30
     ATOM 1752 CB LEU 386
                                64.240 39.434 37.317 1.00 43.34
     ATOM 1753 CG LEU 386
50
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64.559 38.066 37.912 1.00 43.50
    ATOM 1754 CD1 LEU 386
    ATOM 1755 CD2 LEU 386
                                62.946 39.992 37.899 1.00 44.01
                              66.342 42.735 37.405 1.00 40.08
    ATOM 1756 C LEU 386
    ATOM 1757 O LEU 386
                               65.875 43.632 38.112 1.00 42.08
    ATOM 1758 N HIS 387
                              67.643 42.613 37.153 1.00 34.86
    ATOM 1759 CA HIS. 387
                               68.631 43.537 37.700 1.00 39.09
    ATOM 1760 CB HIS 387
                               70.046 43.034 37.421 1.00 39.99
                               70,402 41.791 38.172 1.00 56.37
    ATOM 1761 CG HIS 387
    ATOM 1762 CD2 HIS 387
                               71.384 40.881 37.974 1.00 60.11
                               69.711 41.370 39.290 1.00 60.40
    ATOM 1763 ND1 HIS 387
10
                               70.252 40.255 39.746 1.00 61.89
    ATOM 1764 CE1 HIS 387
                               71.269 39.937 38.966 1.00 63.96
    ATOM 1765 NE2 HIS 387
                              68,446 44.928 37.101 1.00 41.00
    ATOM 1766 C HIS 387
                              68,492 45.927 37.817 1.00 46.99
    ATOM 1767 O HIS 387
                               68.213 44.982 35.792 1.00 39.15
    ATOM 1768 N MET 388
15
    ATOM 1769 CA MET 388
                                68.011 46.243 35.088 1.00 35.32
                                67.676 45.992 33.612 1.00 35.12
    ATOM 1770 CB MET 388
                                68.810 45.442 32.753 1.00 37.24
    ATOM 1771 CG MET 388
    ATOM 1772 SD MET 388
                                68.259 45.150 31.051 1.00 41.75
                                69.274 43.748 30.573 1.00 35.23
    ATOM 1773 CE MET 388
20
                               66.880 47.048 35.733 1.00 36.52
    ATOM 1774 C MET 388
    ATOM 1775 O MET 388
                               66.994 48.265 35.888 1.00 43.39
                               65,792 46.371 36.103 1.00 38.05
    ATOM 1776 N LYS 389
                               64.637 47.025 36.729 1.00 42.88
    ATOM 1777 CA LYS 389
                               63.481 46.035 36.866 1.00 47.83
    ATOM 1778 CB LYS 389
25
    ATOM 1779 CG LYS 389
                               62.835 45.627 35.560 1.00 52.36
    ATOM 1780 CD LYS 389
                                62.040 44.340 35.731 1.00 61.84
                               60.978 44.451 36.814 1.00 69.04
    ATOM 1781 CE LYS 389
                               60.254 43.162 36.987 1.00 70.00
    ATOM 1782 NZ LYS 389
                               64.983 47.587 38.107 1.00 43.99
    ATOM 1783 C LYS 389
30
                               64.455 48.621 38.525 1.00 44.22
    ATOM 1784 O LYS 389
                               65.851 46.878 38.816 1.00 45.50
    ATOM 1785 N VAL 390
                                66.290 47.286 40.142 1.00 47.76
    ATOM 1786 CA VAL 390
                                67.152 46.186 40.804 1.00 46.30
    ATOM 1787 CB VAL 390
                                67.796 46.706 42.079 1.00 49.20
    ATOM 1788 CG1 VAL 390
35
                                66.305 44.962 41.097 1.00 42.69
    ATOM 1789 CG2 VAL 390
                               67.109 48.571 40.070 1.00 47.25
    ATOM 1790 C VAL 390
    ATOM 1791 O VAL 390
                               66.811 49.540 40.760 1.00 48.67
                               68.115 48.580 39.199 1.00 44.11
    ATOM 1792 N GLU 391
    ATOM 1793 CA GLU 391
                                69.009 49.721 39.047 1.00 45.79
                                70.266 49.311 38.273 1.00 45.78
    ATOM 1794 CB GLU 391
                                70.998 48.091 38.830 1.00 57.29
    ATOM 1795 CG GLU 391
                                71.479 48.268 40.261 1.00 61.20
    ATOM 1796 CD GLU 391
    ATOM 1797 OE1 GLU 391
                                71.845 49.400 40.646 1.00 57.29
    ATOM 1798 OE2 GLU 391
                                71.496 47.263 41.001 1.00 63.69
    ATOM 1799 C GLU 391
                               68.410 50.959 38.391 1.00 49.16
    ATOM 1800 O GLU 391
                               68.463 52.055 38.956 1.00 58.82
     ATOM 1801 N CYA 392
                               67.802 50.782 37.224 1.00 49.75
                                67.255 51.908 36.475 1.00 45.56
     ATOM 1802 CA CYA 392
                               67.667 51.768 35.016 1.00 44.82
    ATOM 1803 CB CYA 392
50
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	ATOM	1804 SG CYA 392	69.443 51.771 34.913 1.00 50.78
•	ATOM	1805 AS CYA 392	69.929 50.778 33.022 1.00 53.29
	ATOM	1806 C CYA 392	65.771 52.200 36.601 1.00 44.35
	ATOM	1807 O CYA 392	64.988 51.324 36.962 1.00 44.10
5	ATOM	1808 N PRO 393	65.378 53.469 36.365 1.00 45.52
	ATOM	1809 CD PRO 393	66.275 54.603 36.075 1.00 37.38
	ATOM	1810 CA PRO 393	63.982 53.916 36.444 1.00 45.41
	ATOM	1811 CB PRO 393	64.105 55.438 36.376 1.00 43.33
	ATOM	1812 CG PRO 393	65.329 55.644 35.542 1.00 39.89
10	ATOM	1813 C PRO 393	63.108 53.376 35.318 1.00 44.89
	ATOM	1814 O PRO 393	63.556 53.239 34.175 1.00 45.60
	ATOM	1815 N THR 394	61.843 53.135 35.647 1.00 47.52
	ATOM	1816 CA THR 394	60.853 52.603 34.713 1.00 53.06
	ATOM	1817 CB THR 394	59.459 52.583 35.371 1.00 61.06
15	ATOM	1818 OG1 THR 394	59.609 52.470 36.794 1.00 72.44
	ATOM	1819 CG2 THR 394	58.640 51.401 34.860 1.00 61.05
	ATOM	1820 C THR 394	60.767 53.373 33.392 1.00 49.98
	ATOM	1821 O THR 394	60.507 52.786 32.339 1.00 51.06
	ATOM	1822 N GLU 395	61.024 54.676 33.452 1.00 48.55
20	ATOM	1823 CA GLU 395	60.970 55.548 32.282 1.00 44.21
	ATOM	1824 CB GLU 395	61.258 56.987 32.697 1.00 41.66
	ATOM	1825 C GLU 395	61.899 55.134 31.134 1.00 43.46
	ATOM	1826 O GLU 395	61.684 55.527 29.988 1.00 44.17
	ATOM	1827 N LEU 396	62.934 54.359 31.449 1.00 41.05
25	ATOM	1828 CA LEU 396	63.898 53.899 30.448 1.00 39.55
	ATOM	1829 CB LEU 396	65.270 53.708 31.106 1.00 35.03
	ATOM	1830 CG LEU 396	66.296 54.834 30.945 1.00 40.06
	ATOM	1831 CD1 LEU 396	65.638 56.200 31.055 1.00 39.06
	ATOM	1832 CD2 LEU 396	67.398 54.669 31.978 1.00 32.78
30	ATOM	1833 C LEU 396	63.468 52.602 29.757 1.00 38.50
	ATOM	1834 O LEU 396	64.106 52.150 28.804 1.00 34.72
	ATOM	1835 N PHE 397	62.364 52.028 30.225 1.00 38.76
	ATOM	1836 CA PHE 397	61.860 50.774 29.683 1.00 36.57
	ATOM	1837 CB PHE 397	61.610 49.775 30.819 1.00 33.96
35	ATOM	1838 CG PHE 397	62.842 49.421 31.607 1.00 36.95
	ATOM	1839 CD1 PHE 397	63.331 50.280 32.587 1.00 34.61
	ATOM	1840 CD2 PHE 397	63.523 48.234 31.362 1.00 37.14
	ATOM	1841 CE1 PHE 397	64.481 49.964 33.310 1.00 31.57
	ATOM	1842 CE2 PHE 397	64.675 47.908 32.082 1.00 37.85
40	ATOM	1843 CZ PHE 397	65.153 48.776 33.056 1.00 33.08
	ATOM	1844 C PHE 397	60.584 50.921 28.858 1.00 35.65
	ATOM	1845 O PHE 397	59.519 51.249 29.399 1.00 35.75
	ATOM	1846 N PRO 398	60.672 50.685 27.536 1.00 35.78
	ATOM	1847 CD PRO 398	61.891 50,367 26.767 1.00 32.81
45	ATOM	1848 CA PRO 398	59.503 50.786 26.658 1.00 33.94
	ATOM	1849 CB PRO 398	60.041 50.297 25.315 1.00 33.91
	ATOM	1850 CG PRO 398	61.488 50.707 25.356 1.00 33.09
	ATOM	1851 C PRO 398	58.434 49.840 27.210 1.00 34.98
	ATOM	1852 O PRO 398	58.753 48.729 27.654 1.00 35.76
50	ATOM	1853 N PRO 399	57.163 50.267 27.219 1.00 37.67
			•

	ATOM	1854 CD PRO 399	56.661 51.578 26.776 1.00 38.02
	ATOM	1855 CA PRO 399	56.070 49.433 27.733 1.00 36.86
	ATOM	1856 CB PRO 399	54.803 50.183 27.291 1.00 34.14
	ATOM	1857 CG PRO 399	55.282 51.240 26.310 1.00 37.00
5	ATOM	1858 C PRO 399	56.085 47.970 27.273 1.00 37.06
	ATOM	1859 O PRO 399	55.967 47.063 28.099 1.00 37.07
	ATOM	1860 N LEU 400	56.299 47.738 25.980 1.00 35.13
	ATOM	1861 CA LEU 400	56.327 46.374 25.445 1.00 35.86
	ATOM	1862 CB LEU 400	56.314 46.385 23.914 1.00 31.49
10	ATOM	1863 CG LEU 400	56.181 45.017 23.227 1.00 30.73
	ATOM	1864 CD1 LEU 400	54.901 44.330 23.674 1.00 21.35
	ATOM	1865 CD2 LEU 400	56.197 45.183 21.720 1.00 25.42
	ATOM	1866 C LEU 400	57.542 45.597 25.958 1.00 36.51
	ATOM	1867 O LEU 400	57.458 44.392 26.219 1.00 37.47
15	ATOM	1868 N PHE 401	58.671 46.290 26.095 1.00 32.26
-	ATOM	1869 CA PHE 401	59.899 45.682 26.596 1.00 35.15
	ATOM	1870 CB PHE 401	61.014 46.739 26.648 1.00 35.99
	ATOM	1871 CG PHE 401	62.346 46.213 27.117 1.00 39.41
	ATOM	1872 CD1 PHE 401	62.845 45.003 26.639 1.00 35.94
20	ATOM	1873 CD2 PHE 401	63.119 46.944 28.019 1.00 40.55
	ATOM	1874 CE1 PHE 401	64.088 44.531 27.055 1.00 30.16
	ATOM	1875 CE2 PHE 401	64.367 46.478 28.439 1.00 35.53
	ATOM	1876 CZ PHE 401	64.849 45.271 27.952 1.00 36.39
	ATOM	1877 C PHE 401	59.607 45.129 27.996 1.00 36.42
25	ATOM	1878 O PHE 401	59.957 43.995 28.317 1.00 36.71
	ATOM	1879 N LEU 402	58.920 45.925 28.805 1.00 36.59
	ATOM	1880 CA LEU 402	58.561 45.528 30.158 1.00 37.68
	ATOM	1881 CB LEU 402	57.986 46.720 30.917 1.00 40.71
	ATOM	1882 CG LEU 402	58.963 47.751 31.463 1.00 43.13
30	ATOM	1883 CD1 LEU 402	58.180 48.926 32.031 1.00 39.88
	ATOM	1884 CD2 LEU 402	59.847 47.103 32.527 1.00 38.39
	ATOM	1885 C LEU 402	57.521 44.420 30.164 1.00 38.02
	ATOM	1886 O LEU 402	57.582 43.507 30.984 1.00 37.39
	ATOM	1887 N GLU 403	56.558 44.522 29.251 1.00 39.74
35	ATOM	1888 CA GLU 403	55.469 43.559 29.166 1.00 42.79
	ATOM	1889 CB GLU 403	54.445 44.022 28.129 1.00 46.21
	ATOM	1890 CG GLU 403	53.092 43.330 28.232 1.00 56.88
	ATOM	1891 CD GLU 403	52.090 43.833 27.202 1.00 65.21
	ATOM	1892 OE1 GLU 403	52.230 44.983 26.728 1.00 70.60
40	ATOM	1893 OE2 GLU 403	51.154 43.073 26.870 1.00 70.53
	ATOM	1894 C GLU 403	55.890 42.121 28.886 1.00 40.14
	ATOM	1895 O GLU 403	55.368 41.200 29.506 1.00 40.57
	ATOM	1896 N VAL 404	56.835 41.932 27.966 1.00 39.43
	ATOM	1897 CA VAL 404	57.292 40.586 27.610 1.00 40.96
45	ATOM	1898 CB VAL 404	57.851 40.516 26.159 1.00 35.50
	ATOM	1899 CG1 VAL 404	56.807 40.995 25.177 1.00 43.46
	ATOM	1900 CG2 VAL 404	59.132 41.321 26.030 1.00 25.74
	ATOM	1901 C VAL 404	58.317 39.946 28.536 1.00 41.94
	ATOM	1902 O VAL 404	58.468 38.722 28.533 1.00 43.82
50	ATOM	1903 N PHE 405	59.026 40.759 29.310 1.00 39.84

	ATOM	1904 CA PHE 405	60.051 40.223 30.189 1.00 42.73
	ATOM	1905 CB PHE 405	61.401 40.897 29.913 1.00 36.85
	ATOM	1906 CG PHE 405	61.963 40.596 28.551 1.00 33.23
	ATOM	1907 CD1 PHE 405	62.283 41.625 27.672 1.00 33.90
5	ATOM	1908 CD2 PHE 405	62.157 39.281 28.138 1.00 31.62
	ATOM	1909 CE1 PHE 405	62.786 41.351 26.399 1.00 39.16
	ATOM	1910 CE2 PHE 405	62.657 38.997 26.872 1.00 33.33
	ATOM	1911 CZ PHE 405	62.972 40.033 25.999 1.00 31.99
	ATOM	1912 C PHE 405	59.723 40.273 31.676 1.00 43.97
10	ATOM	1913 O PHE 405	60.636 39.943 32.460 1.00 46.56
	ATOM	1 O1 HOH 501	67.928 36.755 11.188 1.00 33.04
	ATOM	2 O1 HOH 502	69.618 40.719 13.009 1.00 23.00
	ATOM	3 O1 HOH 503	64.885 40.168 12.340 1.00 23.00
	ATOM	4 O1 HOH 504	63.079 40.108 15.841 1.00 23.00
15	ATOM	5 O1 HOH 505	63.404 46.536 15.354 1.00 36.41
	ATOM	6 O1 HOH 506	61.299 15.617 -0.595 1.00 23.00
	ATOM	7 O1 HOH 507	67.359 15.375 0.551 1.00 23.00
	ATOM	8 O1 HOH 508	67.230 12.002 -0.634 1.00 23.00
	ATOM	9 O1 HOH 509	66.906 12.467 3.855 1.00 23.00
20	ATOM	10 O1 HOH 510	61.785 9.946 3.983 1.00 23.00
	ATOM	11 O1 HOH 511	57.670 11.385 9.909 1.00 23.00
	ATOM	12 O1 HOH 512	55.791 11.570 10.291 1.00 23.00
	ATOM	13 O1 HOH 513	54.637 14.058 9.201 1.00 23.00
	ATOM	14 O1 HOH 514	55.882 16.054 12.204 1.00 26.53
25	ATOM	15 O1 HOH 515	53.685 15.842 18.209 1.00 23.00
	ATOM	16 O1 HOH 516	49.559 24.773 19.020 1.00 23.00
	ATOM	17 O1 HOH 517	51.258 25.512 13.384 1.00 37.74
	ATOM	18 O1 HOH 518	53.551 25.749 10.593 1.00 42.31
	ATOM	19 O1 HOH 519	50.338 23.299 7.662 1.00 41.19
30	ATOM	20 O1 HOH 520	50.830 20.272 8.323 1.00 28.46
	ATOM	21 O1 HOH 521	48.630 20.291 6.429 1.00 23.00
	ATOM	22 O1 HOH 522	49.233 17.389 2.867 1.00 23.00
	ATOM	23 O1 HOH 523	52.076 22.770 1.260 1.00 23.00
	ATOM	24 O1 HOH 524	51.671 23.621 -1.020 1.00 23.00
35	ATOM	25 O1 HOH 525	58.294 31.509 2.147 1.00 31.83
	ATOM	26 O1 HOH 526	57.497 36.071 2.268 1.00 23.00
	ATOM	27 O1 HOH 527	65.373 36.025 6.809 1.00 23.00
	ATOM	28 O1 HOH 528	67.871 36.399 6.419 1.00 66.52
	ATOM	29 OI HOH 529	67.189 33.811 9.409 1.00 23.00
40	ATOM	30 O1 HOH 530	62.458 48.056 13.590 1.00 23.00
	ATOM	31 O1 HOH 531	63.943 46.824 10.638 1.00 39.26
	ATOM	32 O1 HOH 532	57.465 45.867 13.186 1.00 23.00
	ATOM	33 O1 HOH 533	55.223 40.774 10.959 1.00 23.00
	ATOM	34 O1 HOH 534	53.737 44.032 19.560 1.00 23.00
45	ATOM	35 O1 HOH 535	55.982 49.757 24.168 1.00 23.00
	ATOM	36 O1 HOH 536	58.575 52.330 31.881 1.00 23.00
	ATOM	37 O1 HOH 537	62.563 49.327 37.804 1.00 23.00
	ATOM	38 O1 HOH 538	61.736 40.280 35.059 1.00 60.53
	ATOM	39 O1 HOH 539	63.271 38.155 34.156 1.00 52.21
50	ATOM	40 O1 HOH 540	61.872 35.187 29.990 1.00 23.00

	ATOM	41 O1 HOH	541	63.701 36.808 28.720 1.00 23.00
	ATOM	42 O1 HOH	542	62.255 35.864 26.425 1.00 26.69
	ATOM	43 O1 HOH	543	63.567 33.453 25.308 1.00 44.90
	ATOM	44 O1 HOH	544	65.456 30.135 27.713 1.00 23.00
5	ATOM	45 O1 HOH	545	61.997 26.566 24.157 1.00 23.00
-	ATOM	46 O1 HOH	546	61.422 22.231 24.358 1.00 23.00
	ATOM	47 O1 HOH	547	59.636 21.462 25.378 1.00 23.00
	ATOM	48 O1 HOH	548	64.860 21.210 22.578 1.00 23.00
	ATOM	49 O1 HOH	549	63.316 14.964 15.508 1.00 52.55
10	ATOM	50 O1 HOH	550	62.770 10.707 15.710 1.00 48.78
10	ATOM	51 O1 HOH	551	61.579 9.665 12.081 1.00 23.00
	ATOM	52 O1 HOH	552	65.916 11.929 11.639 1.00 23.00
	ATOM	53 O1 HOH	553	68.086 12.882 11.226 1.00 23.00
	ATOM	54 O1 HOH	554	69.504 11.968 14.083 1.00 23.00
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13	ATOM	56 O1 HOH	556	74.716 15.172 10.253 1.00 23.00
	ATOM	57 O1 HOH	557	73.109 17.916 7.451 1.00 23.00
	ATOM	58 O1 HOH	558	71.316 15.446 7.652 1.00 23.00
	ATOM	59 O1 HOH	559	74.717 14.555 5.957 1.00 23.00
20	ATOM	60 O1 HOH	560	73.523 22.311 2.467 1.00 23.00
20	ATOM	61 O1 HOH	561	76.491 23.094 5.700 1.00 51.34
	ATOM	62 O1 HOH	562	73.961 29.841 10.035 1.00 33.87
	ATOM	63 O1 HOH	563	76.164 33.031 11.370 1.00 23.00
	ATOM	64 O1 HOH	564	77.193 34.039 9.712 1.00 37.14
25	ATOM	65 O1 HOH	565	76.525 41.395 10.460 1.00 23.00
23	ATOM	66 O1 HOH	566	79.358 49.535 15.048 1.00 53.78
	ATOM	67 O1 HOH	567	78.046 53.530 9.188 1.00 23.00
			568	68.058 52.158 15.548 1.00 23.00
	ATOM		569	
20	ATOM		570	68.598 53.164 18.083 1.00 45.72 73.482 58.914 21.552 1.00 58.99
30	ATOM			
	ATOM		571	65.648 53.551 26.240 1.00 23.00 75.776 46.207 30.367 1.00 33.32
	ATOM		572	78.686 46.470 31.087 1.00 23.00
	ATOM	73 O1 HOH	573	77.580 41.209 31.884 1.00 23.00
25	ATOM	74 O1 HOH	574 575	76.879 31.531 24.067 1.00 23.00
35	ATOM	75 O1 HOH	575	
	ATOM	76 O1 HOH	576	
	ATOM	77 O1 HOH	577	
	ATOM	78 O1 HOH	578	80.631 25.802 15.508 1.00 23.00
40	ATOM	79 O1 HOH	579	82.104 22.566 14.156 1.00 23.00
40	ATOM	80 O1 HOH	580	76.954 22.077 18.425 1.00 46.50
	ATOM	81 O1 HOH	581	86.619 37.903 16.945 1.00 47.66
	ATOM	82 O1 HOH	582	83.586 42.305 18.576 1.00 23.00
	ATOM	83 O1 HOH	583	83.481 45.262 19.526 1.00 23.00
	ATOM	84 O1 HOH	584	66.787 32.864 33.796 1.00 23.00
45	ATOM	85 O1 HOH	585	59.447 33.572 30.734 1.00 23.00
	ATOM	86 O1 HOH	586	57.013 32.278 31.125 1.00 23.00
	ATOM	87 O1 HOH	587	58.084 29.428 24.648 1.00 24.06
	ATOM	88 O1 HOH	588	52.774 25.054 32.650 1.00 57.81
	ATOM	89 O1 HOH	589	53.800 24.465 34.834 1.00 23.00
50	ATOM	90 O1 HOH	590	47.195 30.205 30.414 1.00 23.00

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    ATOM
             93 O1 HOH 593
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             95 O1 HOH 595
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    ATOM
             98 O1 HOH 598
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    ATOM
             99 O1 HOH 599
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    ATOM 102 O1 HOH 602
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                                47.359 19.644 28.494 1.00 41.57
    ATOM 103 O1 HOH 603
    ATOM 2300 C ACY 701
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    ATOM 2301 O ACY 701
                                52.351 40.361 25.771 1.00 48.92
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     ATOM 2302 OXT ACY 701
                                 51.543 40.314 23.527 1.00 41.32
    ATOM 2303 CH3 ACY 701
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     ATOM 2305 C2 IBR
     ATOM 2306 C3 IBR
                              67.192 43.467 19.068 1.00 25.49
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     ATOM 2307 C4 IBR
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                          1
                              67.884 43.772 20.218 1.00 35.08
     ATOM 2308 C5 IBR
                          1
     ATOM 2309 C6 IBR
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                              68.673 42.828 20.790 1.00 30.76
     ATOM 2310 C7 IBR
                              67.681 43.327 25.704 1.00 29.18
     ATOM 2311 C8 IBR
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     ATOM 2312 C9 IBR
     ATOM 2313 C10 IBR
                          1
                              67.383 42.244 24.921 1.00 26.78
                               68.122 41.241 19.099 1.00 25.50
     ATOM 2314 C11 IBR
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     ATOM 2315 C12 IBR
                               66.529 41.932 17.285 1.00 17.69
     ATOM 2316 C13 IBR
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                               68.730 45.450 26.287 1.00 30.43
     ATOM 2317 C14 IBR
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     ATOM 2318 C15 IBR
     ATOM 2319 C16 IBR
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     ATOM 2320 C17 IBR
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                               70.126 46.087 26.069 1.00 26.02
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     ATOM 2321 C18 IBR
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     ATOM 2322 BR1 IBR
                           1
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     ATOM 2323 BR2 IBR
                           1
                              68.284 40.938 15.821 1.00 18.75
     ATOM 2324 N1 IBR
                              67.068 43.397 26.981 1.00 26.31
     ATOM 2325 O1 IBR
                          1
     ATOM 2326 O2 IBR
                         1
                              69.393 43.153 21.933 1.00 30.15
40
                              66.368 40.592 14.004 1.00 23.29
     ATOM 2327 O3 IBR
                         · 1
                              64.786 40.511 15.515 1.00 23.47
     ATOM 2328 O4 IBR
                         1
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     END
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APPENDIX 6

TR_T3.PDB

REMARK rTR_t3 full length numbering

REMARK

5 REMARK Rfactor 0.221 Rfree 0.240

REMARK Resolution 5. 2.0 all reflections

REMARK conformation of MET 388 confirmed by SA_omit map

REMARK

REMARK Three cacodylate-modified cysteines (CYA)

10 REMARK Cya334, Cya380, Cya392

REMARK cacodylate modeled as single arsenic atom

REMARK

REMARK side chain of certain residues modeled as ALA due to poor density;

REMARK however, residue name reflects true residue for clarity

15 REMARK

REMARK clone obtained from Murray et. al.

REMARK deposited sequence confirmed,

REMARK differing from that reported by Thompson et. al.

REMARK in the following codons:

20 REMARK 281 Thr - Ala

REMARK 285 Lys - Glu

REMARK identical to that reported by Mitsuhashi et. al.

REMARK gb:RNTRAVI X07409

JRNL AUTH M.B. MURRAY, N.D.ZILZ,

25 N.L.MCCREARY, M.J.MACDONALD

JRNL AUTH 2 H.C.TOWLE

JRNL TITL ISOLATION AND CHARACTERIZATION OF RAT CDNA CLONES FOR TWO

JRNL TITL 2 DISTINCT THYROID HORMONE RECPTORS

30 JRNL REF JBC

V. 263 25 1988

JRNL AUTH C.C.THOMPSON, C.WEINBERGER, R.LEBO, R.M.EVANS

JRNL TITL IDENTIFICATION OF A NOVEL THYROID HORMONE RECEPTOR EXPRESSED

JRNL TITL 2 IN THE MAMMALIAN CENTRAL NERVOUS SYSTEM

35 JRNL REF SCIENCE V. 237 1987

JRNL AUTH T.MITSUHASHI,G.TENNYSON,V.NIKODEM

JRNL TITL NUCLEOTIDE SEQUENCE OF NOVEL CDNAS GENERATED BY ALTERNATIVE

JRNL TITL 2 SPLICING OF A RAT THYROID HORMONE RECEPTOR

40 GENE TRANSCRIPT

JRNL REF NUC. ACIDS. RES. V. 16 12 1988

REMARK

ATOM 1 CB ARG 157 68.406 10.620 7.027 1.00 41.66

ATOM 2 CG ARG 157 69.926 10.540 6.997 1.00 44.48

45 ATOM 3 CD ARG 157 70.552 11.261 8.173 1.00 47.02

ATOM 4 NE ARG 157 70.112 10.680 9.435 1.00 49.73

ATOM 5 CZ ARG 157 70.917 10.392 10.450 1.00 51.21

ATOM 6 NH1 ARG 157 72.223 10.629 10.361 1.00 51.79

	ATOM	7 NH2 ARG 157	70.405 9.871 11.556 1.00 51.92
	ATOM	8 C ARG 157	66.308 9.993 5.774 1.00 36.48
	ATOM	9 O ARG 157	66.047 10.318 4.622 1.00 38.84
	ATOM	10 N 'ARG 157	68.479 9.473 4.839 1.00 41.22
5	ATOM	11 CA ARG 157	67.734 9.580 6.135 1.00 39.98
	ATOM	12 N PRO 158	65.366 9.953 6.728 1.00 33.85
	ATOM	13 CD PRO 158	65.494 9.553 8.139 1.00 34.72
	ATOM	14 CA PRO 158	63.981 10.336 6.407 1.00 31.89
	ATOM	15 CB PRO 158	63.219 10.015 7.694 1.00 31.87
10	ATOM	16 CG PRO 158	64.260 10.158 8.759 1.00 33.55
	ATOM	17 C PRO 158	63.758 11.783 5.947 1.00 29.77
	ATOM	18 O PRO 158	64.221 12.739 6.575 1.00 27.93
	ATOM	19 N GLU 159	63.071 11.918 4.819 1.00 26.20
	ATOM	20 CA GLU 159	62.759 13.217 4.239 1.00 24.07
15	ATOM	21 CB GLU 159	62.565 13.080 2.721 1.00 22.90
	ATOM	22 CG GLU 159	63.847 12.933 1.916 1.00 22.04
	ATOM	23 CD GLU 159	64.386 14.260 1.427 1.00 22.07
	ATOM	24 OE1 GLU 159	63.577 15.175 1.203 1.00 24.63
	ATOM	25 OE2 GLU 159	65.612 14.389 1.240 1.00 23.54
20	ATOM	26 C GLU 159	61.463 13.717 4.855 1.00 21.56
	ATOM	27 O GLU 159	60.747 12.958 5.516 1.00 21.03
	ATOM	28 N PRO 160	61.176 15.022 4.713 1.00 19.69
	ATOM	29 CD PRO 160	61.997 16.139 4.207 1.00 16.57
	ATOM	30 CA PRO 160	59.923 15.500 5.292 1.00 18.12
25	ATOM	31 CB PRO 160	59.935 16.990 4.955 1.00 15.65
	ATOM	32 CG PRO 160	61.390 17.328 4.905 1.00 14.83
	ATOM	33 C PRO 160	58.741 14.782 4.626 1.00 19.79
	ATOM	34 O PRO 160	58.793 14.431 3.445 1.00 20.20
	ATOM	35 N THR 161	57.713 14.497 5.412 1.00 20.15
30	ATOM	36 CA THR 161	56.525 13.846 4.901 1.00 20.73
	ATOM	37 CB THR 161	55.672 13.274 6.060 1.00 20.77
	ATOM	38 OG1 THR 161	55.195 14.348 6.881 1.00 21.74
	ATOM	39 CG2 THR 161	56.489 12.324 6.917 1.00 19.52
25	ATOM	40 C THR 161	55.724 14.954 4.219 1.00 21.64 56.010 16.139 4.421 1.00 23.13
35	ATOM ATOM	41 O THR 161	
	ATOM	42 N PRO 162 43 CD PRO 162	54.701 14.596 3.425 1.00 21.21 54.309 13.235 3.012 1.00 19.57
	ATOM	44 CA PRO 162	53.884 15.602 2.751 1.00 21.01
	ATOM	45 CB PRO 162	52.722 14.776 2.223 1.00 19.74
40	ATOM	46 CG PRO 162	53.387 13.490 1.861 1.00 20.34
40	ATOM	47 C PRO 162	53.391 16.643 3.753 1.00 22.52
	ATOM	48 O PRO 162	53.508 17.851 3.526 1.00 21.68
	ATOM	49 N GLU 163	52.880 16.151 4.878 1.00 23.01
	ATOM	50 CA GLU 163	52.349 16.996 5.941 1.00 25.97
45	ATOM	51 CB GLU 163	51.672 16.148 7.022 1.00 29.50
7,5	ATOM	52 CG GLU 163	50.476 15.312 6.543 1.00 37.07
	ATOM	53 CD GLU 163	50.865 14.159 5.614 1.00 41.36
	ATOM	54 OE1 GLU 163	51.937 13.544 5.828 1.00 40.11
	ATOM	55 OE2 GLU 163	50.094 13.874 4.660 1.00 46.16
50	ATOM	56 C GLU 163	53.415 17.879 6.581 1.00 24.92
50	LI OIVI	20 C OFO 103	JJ. 713 17.077 0.301 1.00 27.72

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    ATOM
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             70 CG TRP 165
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             89 N LEU 167
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             93 CD1 LEU 167
    ATOM
             94 CD2 LEU 167
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             98 CA ILE 168
     ATOM
                              58.671 22.771 5.995 1.00 17.54
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     ATOM
            100 CG2 ILE 168
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            102 CD1 ILE 168
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     ATOM
     ATOM 103 C ILE 168
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     ATOM. 105 N HIS 169
                              56.591 24.925 4.996 1.00 22.04
     ATOM 106 CA HIS 169
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     ATOM
            109 CD2 HIS 169
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     ATOM
     ATOM
            110 ND1 HIS 169
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    ATOM
            111 CE1 HIS 169
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                               57.513 23.660 0.772 1.00 20.10
            112 NE2 HIS 169
     ATOM
     ATOM
            113 C HIS 169
                              55.615 27.198 4.959 1.00 20.61
     ATOM
            114 O HIS 169
                              55.979 28.370 4.836 1.00 20.08
            115 N VAL 170
                              54.632 26.821 5.769 1.00 20.01
    ATOM
            116 CA VAL 170
                               53.922 27.785 6.580 1.00 20.52
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    ATOM
            117 CB VAL 170
                               52.816 27.120 7.384 1.00 21.33
    ATOM
                                52.224 28.113 8.366 1.00 22.32
    ATOM 118 CG1 VAL 170
    ATOM 119 CG2 VAL 170
                                51.740 26.608 6.438 1.00 23.27
                              54.891 28.477 7.521 1.00 20.58
    ATOM
            120 C VAL 170
                              54.926 29.704 7.554 1.00 22.32
    ATOM
            121 O VAL 170
15
            122 N ALA 171
                              55.712 27.696 8.230 1.00 18.83
    ATOM
    ATOM
            123 CA ALA 171
                               56.692 28.234 9.182 1.00 18.34
    ATOM
            124 CB ALA 171
                               57.375 27.102 9.946 1.00 17.05
    ATOM
            125 C ALA 171
                              57.733 29.151 8.533 1.00 17.84
                              58.084 30.200 9.091 1.00 18.67
            126 O ALA 171
20
    ATOM
            127 N THR 172
    ATOM
                              58.231 28.756 7.367 1.00 17.81
    ATOM
            128 CA THR 172
                               59.215 29.551 6.639 1.00 18.88
    ATOM
            129 CB THR 172
                               59.726 28.794 5.380 1.00 20.47
                               60.280 27.531 5.776 1.00 21.38
            130 OG1 THR 172
    ATOM
25
    ATOM
                                60.806 29.599 4.648 1.00 20.22
            131 CG2 THR 172
    ATOM 132 C THR 172
                              58.655 30.932 6.251 1.00 19.42
           133 O THR 172
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                              59.320 31.957 6.435 1.00 17.98
            134 N GLU 173
                              57.425 30.970 5.756 1.00 19.97
    ATOM
    ATOM
            135 CA GLU 173
                               56.811 32.236 5.374 1.00 22.51
    ATOM
            136 CB GLU 173
                               55.520 31.981 4.577 1.00 27.26
30
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            137 CG GLU 173
                               54.823 33.244 4.005 1.00 34.96
                               55.690 34.040 3.020 1.00 39.54
    ATOM
            138 CD GLU 173
    ATOM 139 OE1 GLU 173
                               56.610 33.454 2.395 1.00 41.82
    ATOM 140 OE2 GLU 173
                                55.443 35.259 2.872 1.00 41.06
                              56.538 33.099 6.622 1.00 21.60
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    ATOM
            141 C GLU 173
                              56.726 34.313 6.595 1.00 21.73
    ATOM
            142 O GLU 173
    ATOM
            143 N ALA 174
                              56.123 32.461 7.716 1.00 19.69
    ATOM
            144 CA ALA 174
                               55.844 33.155 8.968 1.00 18.07
                               55.423 32.169 10.037 1.00 16.90
    ATOM
            145 CB ALA 174
40
    ATOM
            146 C ALA 174
                              57.101 33.883 9.400 1.00 17.65
                              57.052 35.031 9.829 1.00 19.80
    ATOM
            147 O ALA 174
    ATOM
            148 N HIS 175
                              58.240 33.222 9.259 1.00 16.39
    ATOM
            149 CA HIS 175
                              59.498 33.831 9.629 1.00 16.41
    ATOM
            150 CB HIS 175
                              60.574 32.758 9.804 1.00 12.71
45
    ATOM
            151 CG HIS 175
                              61.938 33.318 10.043 1.00 11.09
                               62.373 34.252 10.920 1.00 8.26
    ATOM
            152 CD2 HIS 175
    ATOM
            153 ND1 HIS 175
                               63.030 32.977 9.273 1.00 13.39
                              64.076 33.683 9.658 1.00 13.77
    ATOM
            154 CE1 HIS 175
    ATOM
            155 NE2 HIS 175
                             63.702 34.464 10.658 1.00 12.70
                             59.959 34.903 8.624 1.00 19.55
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    ATOM 156 C HIS 175
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60.293 36.027 9.016 1.00 18.38
            157 O HIS 175
    ATOM
                              59.987 34.555 7.339 1.00 20.77
    ATOM
            158 N ARG 176
            159 CA ARG 176
                               60.424 35.494 6.307 1.00 21.30
    ATOM
                               60.315 34.876 4.917 1.00 24.87
    ATOM
            160 CB ARG 176
            161 CG ARG 176
                               61.361 33.827 4.609 1.00 30.22
    ATOM
                               61.429 33.603 3.116 1.00 36.29
            162 CD ARG 176
    ATOM
                               62.256 32.457 2.758 1.00 44.72
    ATOM
            163 NE ARG 176
                               62.031 31.680 1.700 1.00 49.80
    ATOM
            164 CZ ARG 176
                                61.000 31.935 0.894 1.00 50.83
            165 NH1 ARG 176
    ATOM
                                62.812 30.627 1.466 1.00 50.14
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    ATOM
            166 NH2 ARG 176
                              59.658 36.807 6.337 1.00 20.67
    ATOM
            167 C ARG 176
            168 O ARG 176
                              60.256 37.877 6.238 1.00 20.53
    ATOM
            169 N SER 177
                              58.344 36.730 6.508 1.00 20.67
    ATOM
                              57.526 37.934 6.551 1.00 21.86
            170 CA SER 177
    ATOM
                              56.061 37.588 6.298 1.00 19.59
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    ATOM
            171 CB SER 177
    ATOM
            172 OG SER 177
                               55.541 36.774 7.329 1.00 21.85
            173 C SER 177
                              57.659 38.733 7.857 1.00 23.27
    ATOM
    ATOM
            174 O SER 177
                              57.073 39.807 7.989 1.00 24.40
            175 N THR 178
                              58.383 38.202 8.837 1.00 22.16
    ATOM
20
    ATOM
            176 CA THR 178
                               58.542 38.913 10.095 1.00 20.62
            177 CB THR 178
                               57.853 38.162 11.265 1.00 19.93
    ATOM
                               58.386 36.838 11.381 1.00 18.72
    ATOM
            178 OGI THR 178
            179 CG2 THR 178
                               56.359 38.057 11.033 1.00 16.95
    ATOM
                              60.015 39.137 10.394 1.00 21.57
    ATOM
            180 C THR 178
25
    ATOM
            181 O THR 178
                              60.368 39.649 11.449 1.00 23.91
                              60.870 38.769 9.445 1.00 22.22
    ATOM
            182 N ASN 179
            183 CA ASN 179
                               62.316 38.912 9.585 1.00 24.22
    ATOM
            184 CB ASN 179
                               63.013 37.690 8.970 1.00 22.49
    ATOM
                               64.480 37.596 9.344 1.00 23.53
    ATOM
            185 CG ASN 179
            186 ODI ASN 179
                               64.866 37.912 10.464 1.00 22.32
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    ATOM
            187 ND2 ASN 179
                               65.296 37.100 8.425 1.00 23.84
    ATOM
    ATOM
            188 C ASN 179
                              62.744 40.210 8.881 1.00 26.52
    ATOM
            189 O ASN 179
                              62.923 40.253 7.657 1.00 26.65
                              62.898 41.267 9.671 1.00 27.47
    ATOM
            190 N ALA 180
                              63.255 42.582 9.166 1.00 30.30
    ATOM
            191 CA ALA 180
35
                               63.552 43.508 10.321 1.00 27.21
    ATOM
            192 CB ALA 180
            193 C ALA 180
                              64.404 42.593 8.166 1.00 33.14
    ATOM
                              65.440 41.972 8.397 1.00 33.71
            194 O ALA 180
    ATOM
    ATOM
            195 N GLN 181
                              64.209 43.295 7.049 0.50 35.09
                                                            ALTA
                               65.212 43.423 5.980 0.50 37.44
40
            196 CA GLN 181
                                                             ALTA
    ATOM
            197 CB GLN 181
                               66.544 43.974 6.511 0.50 38.60
                                                             ALTA
    ATOM
            198 CG GLN 181
                               66.728 45.462 6.299 0.50 40.53
                                                             ALTA
    ATOM
    ATOM
            199 CD GLN 181
                               65.805 46.291 7.162 0.50 42.72
                                                             ALTA
    ATOM
           200 OE1 GLN 181
                               64.639 46.512 6.828 0.50 42.05
                                                             ALTA
                               66.324 46.756 8.284 0.50 44.59
45
    ATOM
           201 NE2 GLN 181
                                                             ALTA
                              65.481 42.180 5.138 0.50 38.43
    ATOM 202 C GLN 181
                                                            ALTA
    ATOM 203 O GLN 181
                              66.175 42.262 4.118 0.50 38.92
                                                            ALTA
    ATOM 204 N GLY 182
                              64,958 41.034 5.562 1.00 38.74
                              65.166 39.808 4.805 1.00 40.07
    ATOM 205 CA GLY 182
                              66.634 39.554 4.486 1.00 42.06
    ATOM 206 C GLY 182
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ATOM
            207 O GLY 182
                              67.504 39.684 5.346 1.00 43.28
            208 N SER 183
                              66.926 39.272 3.224 1.00 43.72
    ATOM
                               68.299 39.001 2.812 1.00 45.88
    ATOM
            209 CA SER 183
            210 CB SER 183
                              68.304 38.069 1.593 1.00 47.26
    ATOM
                               67.519 38.605 0.531 1.00 47.23
            211 OG SER 183
    ATOM
                              69.095 40.268 2.497 1.00 46.24
    ATOM
            212 C SER 183
           213 O SER 183
                              70.290 40.194 2.185 1.00 48.13
    ATOM
            214 N HIS 184
                             68.445 41.426 2.579 1.00 45.79
    ATOM
                              69.111 42.690 2.276 1.00 45.00
            215 CA HIS 184
    ATOM
    ATOM
                              68.127 43.636 1.594 1.00 43.54
            216 CB HIS 184
10
                             69.732 43.351 3.516 1.00 44.67
    ATOM
            217 C HIS 184
    ATOM
            218 O HIS 184
                             70.316 44.440 3.428 1.00 45.02
            219 N TRP 185
                              69.659 42.663 4.653 1.00 43.24
    ATOM
                               70.190 43.172 5.919 1.00 40.98
           220 CA TRP 185
    ATOM
            221 CB TRP 185
                               70.078 42.106 7.020 1.00 37.96
15
    ATOM
                               70.889 40.874 6.775 1.00 34.14
     ATOM
            222 CG TRP 185
    ATOM
           223 CD2 TRP 185
                               72.197 40.593 7.291 1.00 33.38
                               72.572 39.321 6.807 1.00 31.68
           224 CE2 TRP 185
    ATOM
                               73.092 41.296 8.107 1.00 31.65
    ATOM
            225 CE3 TRP 185
                               70.530 39.790 6.028 1.00 34.27
            226 CD1 TRP 185
20
    ATOM
                               71.536 38.852 6.043 1.00 33.51
    ATOM
           227 NE1 TRP 185
    ATOM 228 CZ2 TRP 185
                               73.795 38.733 7.121 1.00 31.67
                               74.308 40.713 8.419 1.00 31.29
            229 CZ3 TRP 185
     ATOM
                               74.651 39.444 7.923 1.00 31.06
    ATOM 230 CH2 TRP 185
                              71.618 43.720 5.856 1.00 41.52
25
    ATOM 231 C TRP 185
    ATOM 232 O TRP 185
                              71.893 44.817 6.335 1.00 40.52
     ATOM 233 N LYS 186
                              72.520 42.976 5.234 1.00 42.94
                               73.896 43.417 5.143 1.00 45.25
    ATOM 234 CA LYS 186
                               74,764 42.328 4.508 1.00 45.96
     ATOM 235 CB LYS 186
     ATOM 236 CG LYS 186
                               76.255 42.600 4.590 1.00 48.07
30
    ATOM 237 CD LYS 186
                               77.053 41.307 4.504 1.00 51.20
                               78.554 41.574 4.457 1.00 52.69
     ATOM 238 CE LYS 186
     ATOM 239 NZ LYS 186
                               78.975 42.277 3.201 1.00 55.56
                              74.025 44.730 4.377 1.00 47.38
     ATOM 240 C LYS 186
                              74.914 45.535 4.663 1.00 47.65
35
     ATOM 241 O LYS 186
                              73.134 44.959 3.418 0.50 48.02
                                                            ALTA
     ATOM 242 N GLN 187
     ATOM 243 CA GLN 187
                               73.193 46.183 2.623 0.50 48.69
                                                             ALTA
                               72.547 45.973 1.246 0.50 48.66
     ATOM 244 CB GLN 187
                                                             ALTA
                               73.104 44.771 0.453 0.50 49.05
                                                             ALTA
     ATOM 245 CG GLN 187
     ATOM 246 CD GLN 187
                               74.624 44.766 0.339 0.50 49.17
                                                             ALTA
40
                                75.225 45.691 -0.209 0.50 49.71
                                                              ALTA
     ATOM 247 OE1 GLN 187
                                75.250 43.710 0.847 0.50 48.57
                                                              ALTA
     ATOM
           248 NE2 GLN 187
     ATOM 249 C GLN 187
                              72.551 47.373 3.343 0.50 49.06
                                                            ALTA
            250 O GLN 187
                               73.094 48.475 3.329 0.50 49.53
                                                            ALTA
     ATOM
                              71.405 47.152 3.980 1.00 49.18
           251 N ARG 188
45
     ATOM
                               70.723 48.221 4.695 1.00 49.90
            252 CA ARG 188
     ATOM
            253 CB ARG 188
                               69.209 47.988 4.653 1.00 53.68
     ATOM
                               68.617 47.798 3.251 1.00 57.22
     ATOM
           254 CG ARG 188
                                67.099 47.962 3.302 1.00 60.67
     ATOM 255 CD ARG 188
     ATOM 256 NE ARG 188
                               66.430 47.441 2.110 1.00 64.43
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65.931 46.208 2.009 1.00 66.13
    ATOM
           257 CZ ARG 188
            258 NH1 ARG 188
                                66.027 45.362 3.031 1.00 66.69
    ATOM
                                65.318 45.823 0.893 1.00 66.10
    ATOM
           259 NH2 ARG 188
                              71.150 48.510 6.133 1.00 48.42
    ATOM 260 C ARG 188
                              70.544 49.368 6.784 1.00 48.86
    ATOM 261 O ARG 188
                              72.153 47.804 6.647 1.00 46.00
    ATOM 262 N ARG 189
                               72.581 48.030 8.028 1.00 44.24
    ATOM 263 CA ARG 189
                               73.039 46.726 8.690 1.00 43.40
    ATOM 264 CB ARG 189
    ATOM 265 CG ARG 189
                               74.367 46.204 8.203 1.00 43.05
                               74.808 45.021 9.019 1.00 43.62
    ATOM 266 CD ARG 189
10
                               76.185 44.660 8.717 1.00 45.95
    ATOM 267 NE ARG 189
                               76.981 43.976 9.536 1.00 48.56
    ATOM 268 CZ ARG 189
                                76,548 43,560 10,724 1,00 46,34
    ATOM 269 NH1 ARG 189
                                78.233 43.735 9.174 1.00 50.12
    ATOM 270 NH2 ARG 189
                              73.642 49.116 8.238 1.00 43.20
    ATOM 271 C ARG 189
15
                              74.629 49.210 7.500 1.00 43.07
    ATOM 272 O ARG 189
                              73.427 49.925 9.268 1.00 41.56
    ATOM 273 N LYS 190
    ATOM 274 CA LYS 190
                               74.335 51.003 9.628 1.00 39.96
                               73,563 52,323 9,757 1.00 38.85
    ATOM 275 CB LYS 190
                              74.983 50.631 10.956 1.00 38.91
    ATOM 276 C LYS 190
20
                              74.345 50.015 11.806 1.00 38.17
    ATOM 277 O LYS 190
    ATOM 278 N PHE 191
                              76.261 50.959 11.104 1.00 38.49
    ATOM 279 CA PHE 191
                               76.998 50.673 12.326 1.00 38.42
                               78.500 50.762 12.073 1.00 38.37
    ATOM 280 CB PHE 191
                               79.056 49.608 11.308 1.00 39.05
25
    ATOM 281 CG PHE 191
                               78.712 49.408 9.976 1.00 40.02
    ATOM 282 CD1 PHE 191
                               79.942 48.727 11.917 1.00 39.19
    ATOM 283 CD2 PHE 191
                               79.245 48.344 9.256 1.00 40.57
    ATOM 284 CE1 PHE 191
                               80.482 47.661 11.213 1.00 40.32
    ATOM 285 CE2 PHE 191
                               80.133 47.466 9.875 1.00 41.84
    ATOM 286 CZ PHE 191
30
                              76.650 51.673 13.416 1.00 37.96
    ATOM 287 C PHE 191
                              76.568 52.872 13.151 1.00 38.95
    ATOM 288 O PHE 191
    ATOM 289 N LEU 192
                              76.433 51.184 14.634 1.00 37.05
                               76.138 52.063 15.759 1.00 35.99
    ATOM 290 CA LEU 192
                               75.833 51.247 17.014 1.00 33.04
    ATOM 291 CB LEU 192
35
                               75.503 52.074 18.260 1.00 31.38
    ATOM 292 CG LEU 192
                                74.116 52.651 18.102 1.00 29.02
    ATOM 293 CD1 LEU 192
                                75.592 51.229 19.536 1.00 30.32
    ATOM 294 CD2 LEU 192
                              77.436 52.831 15.976 1.00 36.99
     ATOM 295 C LEU 192
                              78.500 52.218 16.112 1.00 37.66
40
     ATOM 296 O LEU 192
            297 N PRO 193
                              77.377 54.177 15.988 1.00 38.15
     ATOM
                               76.156 54.996 15.902 1.00 37.90
     ATOM 298 CD PRO 193
                               78.561 55.025 16.187 1.00 38.68
     ATOM 299 CA PRO 193
                               77.950 56.365 16.568 1.00 37.20
     ATOM
            300 CB PRO 193
                               76.711 56.397 15.758 1.00 37.08
45
     ATOM
            301 CG PRO 193
                              79.475 54.503 17.294 1.00 41.12
            302 C PRO 193
     ATOM
                              79.005 54.129 18.367 1.00 42.26
     ATOM
            303 O PRO 193
                              80,782 54,509 17.052 1.00 43.62
     ATOM
            304 N ASP 194
                               81.731 54.012 18.050 1.00 46.71
            305 CA ASP 194
     ATOM
                               83.131 53.938 17.470 1.00 49.32
     ATOM 306 CB ASP 194
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	ATOM ATOM	307 CG ASP 194 308 OD1 ASP 194	83.237 52.904 16.397 1.00 52.34 83.539 51.726 16.719 1.00 53.18
	ATOM	309 OD2 ASP 194	82.981 53.268 15.227 1.00 55.10
	ATOM	310 C ASP 194	81.769 54.743 19.386 1.00 47.12
5	ATOM	311 O ASP 194	82.158 54.163 20.403 1.00 48.16
,	ATOM	312 N ASP 195	81.389 56.015 19.386 1.00 47.54
	ATOM	313 CA ASP 195	81.382 56.791 20.620 1.00 48.68
	ATOM	314 CB ASP 195	81.180 58.285 20.322 1.00 50.76
	ATOM	315 CG ASP 195	79.871 58.572 19.602 1.00 54.24
10	ATOM	316 OD1 ASP 195	78.929 59.082 20.253 1.00 56.17
	ATOM	317 OD2 ASP 195	79.786 58.292 18.385 1.00 56.08
	ATOM	318 C ASP 195	80.304 56.274 21.580 1.00 47.63
	ATOM	319 O ASP 195	80.294 56.621 22.772 1.00 49.07
	ATOM	320 N ILE 196	79.400 55.444 21.065 1.00 44.87
15	ATOM	321 CA ILE 196	78.330 54.890 21.888 1.00 42.53
	ATOM	322 CB ILE 196	76.983 54.813 21.121 1.00 42.19
	ATOM	323 CG2 ILE 196	75.870 54.357 22.060 1.00 40.29
	ATOM	324 CG1 ILE 196	76.635 56.191 20.535 1.00 41.32
	ATOM	325 CD1 ILE 196	75.344 56.219 19.732 1.00 41.32
20	ATOM	326 C ILE 196	78.725 53.509 22.391 1.00 40.89
	ATOM	327 O ILE 196	79.358 52.722 21.679 1.00 40.08
	ATOM	328 N GLY 197	78.384 53.240 23.642 1.00 40.16
	ATOM	329 CA GLY 197	78.705 51.957 24.228 1.00 40.21
	ATOM	330 C GLY 197	80.066 51.907 24.879 1.00 40.18
25	ATOM	331 O GLY 197	80.512 50.839 25.267 1.00 40.55 80.718 53.057 25.029 1.00 41.25
	ATOM	332 N GLN 198 333 CA GLN 198	82.038 53.111 25.664 1.00 40.94
	ATOM ATOM	333 CA GLN 198 334 CB GLN 198	83.041 53.823 24.738 1.00 39.51
	ATOM	334 CB GLN 198	81.995 53.796 27.046 1.00 40.93
30	ATOM	336 O GLN 198	83.036 54.197 27.571 1.00 41.83
30	ATOM	337 N SER 199	80.806 53.859 27.654 1.00 39.68
	ATOM	338 CA SER 199	80.615 54.510 28.961 1.00 37.74
	ATOM	339 CB SER 199	79.995 55.905 28.768 1.00 38.50
	ATOM	340 OG SER 199	80.687 56.672 27.792 1.00 40.71
35	ATOM	341 C SER 199	79.743 53.726 29.958 1.00 36.31
	ATOM	342 O SER 199	78.719 54.228 30.436 1.00 35.69
	ATOM	343 N PRO 200	80.123. 52.484 30.280 1.00 35.05
	ATOM	344 CD PRO 200	81.246 51.684 29.760 1.00 33.97
	ATOM	345 CA PRO 200	79.313 51.715 31.228 1.00 35.89
40	ATOM	346 CB PRO 200	79.872 50.304 31.075 1.00 33.94
	ATOM	347 CG PRO 200	81.297 50.532 30.708 1.00 33.31
	ATOM	348 C PRO 200	79.477 52.241 32.656 1.00 37.75
	ATOM	349 O PRO 200	80.484 51.959 33.299 1.00 38.78
	ATOM	350 N ILE 201	78.493 52.988 33.158 1.00 39.61
45	ATOM	351 CA ILE 201	78.590 53.551 34.511 1.00 40.56
	ATOM	352 CB ILE 201	78.715 55.093 34.484 1.00 40.20
	ATOM	353 CG2 ILE 201	80.125 55.501 34.082 1.00 41.06
	ATOM	354 CG1 ILE 201	77.690 55.694 33.532 1.00 40.98
	ATOM	355 CD1 ILE 201	77.969 57.147 33.205 1.00 44.31
50	ATOM	356 C ILE 201	77.535 53.160 35.546 1.00 41.40

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357 O ILE 201
                              77.768 53.313 36.751 1.00 42.09
    ATOM
                              76.365 52.701 35.104 1.00 41.42
            358 N VAL 202
    ATOM
                               75.325 52.293 36.053 1.00 40.70
    ATOM
            359 CA VAL 202
            360 CB VAL 202
                               73.913 52.292 35.422 1.00 38.44
    ATOM
                                72.881 51.826 36.435 1.00 35.91
    ATOM
            361 CG1 VAL 202
            362 CG2 VAL 202
                                73.560 53.692 34.934 1.00 36.42
    ATOM
                              75.687 50.917 36.622 1.00 41.64
            363 C VAL 202
    ATOM
            364 O VAL 202
                              76.094 50.008 35.894 1.00 42.05
    ATOM
            365 N SER 203
                              75.596 50.800 37.938 1.00 43.06
    ATOM
            366 CA SER 203
                               75.947 49.576 38.639 1.00 44.57
10
    ATOM
                               75.916 49.842 40.154 1.00 46.82
            367 CB SER 203
    ATOM
                              .76.457 48.772 40.916 1.00 50.18
            368 OG SER 203
    ATOM
            369 C SER 203
                              75.052 48.388 38.294 1.00 44.08
    ATOM
                              73,849 48.534 38.093 1.00 44.28
    ATOM
            370 O SER 203
            371 N MET 204
                               75.656 47.210 38.231 1.00 43.11
    ATOM
15
                               74.930 45.980 37.963 1.00 43.12
            372 CA MET 204
    ATOM
            373 CB MET 204
                               75.048 45.557 36.494 1.00 41.07
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            374 CG MET 204
                               74.126 46.320 35.554 1.00 36.96
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            375 SD MET 204
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            376 CE MET 204
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                               75,561 44,943 38,866 1.00 43,68
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                               76.784 44.817 38.912 1.00 44.32
            378 O MET 204
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    ATOM
            379 N PRO 205
                               74.735 44.204 39.619 1.00 44.22
            380 CD PRO 205
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            383 CG PRO 205
            384 C PRO 205
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                              76.417 42.354 40.122 1.00 44.31
            385 O PRO 205
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                               77.073 40.106 37.270 1.00 47.12
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            388 CB ASP 206
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            389 CG ASP 206
            390 OD1 ASP 206
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            391 OD2 ASP 206
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            393 O ASP 206
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                               78.804 43.039 38.145 1.00 44.19
            394 N GLY 207
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                               80.001 43.785 37.803 1.00 43.51
           395 CA GLY 207
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                               80.041 44.425 36.433 1.00 43.29
            396 C GLY 207
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     ATOM
            397 O GLY 207
                               80.745 45.421 36.257 1.00 44.47
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            398 N ASP 208
                              79.363 43.845 35.446 1.00 42.45
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            399 CA ASP 208
                               79.347 44.436 34.106 1.00 41.51
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                               78.915 43.402 33.070 1.00 42.91
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            400 CB ASP 208
            401 CG ASP 208
                               80.001 42.379 32.785 1.00 43.57
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                                79.675 41.218 32.468 1.00 44.55
            402 OD1 ASP 208
     ATOM
                                81.191 42.742 32.868 1.00 47.14
     ATOM 403 OD2 ASP 208
                              78.378 45.606 34.143 1.00 40.78
     ATOM 404 C ASP 208
                              77.176 45.403 34.277 1.00 42.50
            405 O ASP 208
     ATOM
                              78.902 46.827 34.058 1.00 39.10
     ATOM 406 N LYS 209
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                               78.910 49.211 34.681 1.00 37.29
            408 CB LYS 209
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                              77.326 48.423 32.871 1.00 34.47
    ATOM
            409 C LYS 209
                              77.707 48.013 31.776 1.00 33.85
    ATOM
           410 O LYS 209
                               76.275 49.228 33.028 1.00 33.30
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            411 N VAL 210
                               75.448 49.684 31.907 1.00 31.78
           412 CA VAL 210
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                               73.929 49.618 32.235 1.00 29.51
    ATOM 413 CB VAL 210
                                73.102 50.012 31.010 1.00 29.24
    ATOM 414 CG1 VAL 210
                                73.541 48.237 32.698 1.00 29.84
    ATOM 415 CG2 VAL 210
    ATOM 416 C VAL 210
                              75.731 51.115 31.451 1.00 32.68
10
                              75.845 52.033 32.264 1.00 32.69
    ATOM 417 O VAL 210
                              75.769 51.290 30.134 1.00 33.00
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            418 N ASP 211
    ATOM 419 CA ASP 211
                               75.978 52.574 29.476 1.00 31.85
                               76.826 52.353 28.221 1.00 32.38
    ATOM 420 CB ASP 211
    ATOM 421 CG ASP 211
                               77.019 53.612 27.386 1.00 31.88
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                               78.123 53.768 26.843 1.00 32.78
     ATOM 422 OD1 ASP 211
                                76.079 54.412 27.208 1.00 32.32
     ATOM 423 OD2 ASP 211
    ATOM 424 C ASP 211
                              74.562 53.023 29.101 1.00 33.39
                              73.925 52.444 28.206 1.00 31.94
            425 O ASP 211
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                              74.078 54.063 29.770 1.00 32.50
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            426 N LEU 212
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            427 CA LEU 212
                               72.731 54.568 29.532 1.00 32.29
     ATOM
                               72.440 55.736 30.470 1.00 32.41
            428 CB LEU 212
     ATOM
                               72.311 55.336 31.936 1.00 32.11
     ATOM
           429 CG LEU 212
     ATOM 430 CD1 LEU 212
                                72.447 56.555 32.830 1.00 32.35
                                70.979 54.650 32.148 1.00 30.87
     ATOM 431 CD2 LEU 212
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            432 C LEU 212
                              72.419 54.962 28.092 1.00 32.29
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                               71.326 54.695 27.609 1.00 32.13
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            433 O LEU 212
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            434 N GLU 213
                               73,370 55,589 27,407 1.00 32.21
                               73.144 56.007 26.028 1.00 33.12
            435 CA GLU 213
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                               74.305 56.864 25.530 1.00 36.72
     ATOM 436 CB GLU 213
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     ATOM 437 CG GLU 213
                               74.067 57.468 24.146 1.00 40.61
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            438 CD GLU 213
                                76.434 57.851 24.059 1.00 46.23
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            439 OEI GLU 213
            440 OE2 GLU 213
                                75.178 58.836 22.543 1.00 45.81
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                               72.966 54.801 25.111 1.00 31.91
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            441 C GLU 213
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                               72.064 54.775 24.273 1.00 31.31
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            442 O GLU 213
            443 N ALA 214
                               73.827 53.803 25.285 1.00 30.66
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                               73.769 52.585 24.482 1.00 30.43
            444 CA ALA 214
     ATOM
                               74.971 51.690 24.783 1.00 29.77
            445 CB ALA 214
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                               72.464 51.854 24.778 1.00 29.34
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            446 C ALA 214
            447 O ALA 214
                               71.772 51.421 23.862 1.00 28.33
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                               72.116 51.762 26.058 1.00 28.45
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            449 CA PHE 215
                               70.882 51.116 26.492 1.00 29.05
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                               70.732 51.240 28.005 1.00 25.98
            450 CB PHE 215
     ATOM
            451 CG PHE 215
                               69.443 50.689 28.535 1.00 25.53
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     ATOM
                                69.330 49.344 28.854 1.00 26.16
            452 CD1 PHE 215
     ATOM
                                68.349 51.519 28.737 1.00 25.04
     ATOM
            453 CD2 PHE 215
                                68.144 48.831 29.370 1.00 25.73
            454 CEI PHE 215
     ATOM
                                67.160 51.018 29.252 1.00 25.84
            455 CE2 PHE 215
     ATOM
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                               67.058 49.669 29.570 1.00 25.25
     ATOM 456 CZ PHE 215
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                               68.773 51.107 25.316 1.00 30.38
            458 O PHE 215
    ATOM
            459 N SER 216
                               69.714 53.108 25.776 1.00 31.41
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            460 CA SER 216
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    ATOM
            461 CB SER 216
                               68.976 55.375 25.256 1.00 32.50
    ATOM
                               67.972 56.153 24.628 1.00 35.83
    ATOM
            462 OG SER 216
            463 C SER 216
                               68.600 53.504 23.663 1.00 31.67
    ATOM
            464 O SER 216
                               67.527 53.235 23.129 1.00 31.34
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                               69.756 53.475 23.014 1.00 31.72
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                                69.823 53.121 21.609 1.00 33.06
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            466 CA GLU 217
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    ATOM
            467 CB GLU 217
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                                71.824 54.557 20.921 1.00 38.98
            468 CG GLU 217
    ATOM
    ATOM
            469 CD GLU 217
                                70.986 55.399 19.963 1.00 41.92
                                70.177 56.221 20.444 1.00 44.02
            470 OE1 GLU 217
    ATOM
            471 OE2 GLU 217
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            472 C GLU 217
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            473 O GLU 217
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            474 N PHE 218
                               69.477 50.779 22.181 1.00 29.80
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    ATOM
            475 CA PHE 218
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            476 CB PHE 218
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                                71.114 48.292 22.467 1.00 24.76
            477 CG PHE 218
    ATOM
                                72.083 48.191 23.446 1.00 24.37
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            478 CD1 PHE 218
                                71.510 48.354 21.134 1.00 24.30
    ATOM
            479 CD2 PHE 218
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    ATOM
            480 CE1 PHE 218
            481 CE2 PHE 218
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                               73.804 48.236 21.772 1.00 24.45
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            483 C PHE 218
                               67.441 49.403 22.255 1.00 26.94
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                               66.658 48.985 21.409 1.00 27.98
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            484 O PHE 218
                               67.032 49.906 23.405 1.00 26.97
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            485 N THR 219
            486 CA THR 219
                                65.619 49.876 23.740 1.00 27.25
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    ATOM
                                65.379 50.304 25.195 1.00 27.35
            487 CB THR 219
    ATOM
            488 OG1 THR 219
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            489 CG2 THR 219
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    ATOM
    ATOM
            490 C THR 219
                               64.747 50.689 22.782 1.00 27.21
                               63.588 50.348 22.557 1.00 28.58
            491 O THR 219
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            492 N LYS 220
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            493 CA LYS 220
            494 CB LYS 220
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            495 C LYS 220
                               64.058 51.772 20.056 1.00 28.62
                               63.014 52.101 19.500 1.00 28.63
            496 O LYS 220
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            497 N ILE 221
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            498 CA ILE 221
                               64.331 49.907 18.527 1.00 28.19
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            499 CB ILE 221
            500 CG2 ILE 221
                               65.866 51.095 16.911 1.00 26.61
     ATOM
            501 CG1 ILE 221
                                66.645 48.977 18.061 1.00 26.80
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     ATOM
            502 CD1 ILE 221
                               67.621 48.417 17.029 1.00 24.91
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                              63.840 48.512 18.937 1.00 28.82
     ATOM
            503 C ILE 221
            504 O ILE 221
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            505 N ILE 222
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     ATOM 506 CA ILE 222
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            508 CG2 ILE 222
    ATOM
                               63.949 45.065 22.230 1.00 24.15
     ATOM 509 CG1 ILE 222
    ATOM 510 CD1 ILE 222
                               64.727 44.610 23.458 1.00 21.43
           511 C ILE 222
                             61.797 46.614 20.519 1.00 28.33
    ATOM
     ATOM 512 O ILE 222
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    ATOM 513 N THR 223
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                               59.494 47.366 20.505 1.00 26.83
    ATOM 514 CA THR 223
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    ATOM 515 CB THR 223
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    ATOM 516 OG1 THR 223
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                                57.183 48.390 20.525 1.00 26.50
    ATOM 517 CG2 THR 223
                              59.103 46.698 19.183 1.00 25.28
    ATOM 518 C THR 223
    ATOM 519 O THR 223
                              58.390 45.691 19.196 1.00 24.87
     ATOM 520 N PRO 224
                              59.535 47.256 18.031 1.00 23.96
    ATOM 521 CD PRO 224
                               60.138 48.580 17.792 1.00 22.28
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                               59.181 46.612 16.759 1.00 23.13
    ATOM 522 CA PRO 224
    ATOM 523 CB PRO 224
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    ATOM
           524 CG PRO 224
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    ATOM 525 C PRO 224
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     ATOM 526 O PRO 224
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                               61.622 43.684 17.213 1.00 18.54
           528 CA ALA 225
    ATOM
     ATOM 529 CB ALA 225
                               63.009 43.773 17.806 1.00 16.79
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           531 O ALA 225
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     ATOM
                              60.253 43.033 19.117 1.00 18.30
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     ATOM
     ATOM 533 CA ILE 226
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     ATOM 534 CB ILE 226
                              59.092 42.779 21.288 1.00 17.30
                               58.057 41.952 22.020 1.00 17.76
     ATOM 535 CG2 ILE 226
                               60.361 42.915 22.123 1.00 17.07
     ATOM 536 CG1 ILE 226
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     ATOM 537 CD1 ILE 226
                               60.175 43.775 23.351 1.00 14.65
                              58,109 41.858 19.199 1.00 19.56
     ATOM 538 C ILE 226
                              57.638 40.719 19.163 1.00 19.51
     ATOM 539 O ILE 226
     ATOM 540 N THR 227
                               57.521 42.903 18.627 1.00 20.26
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     ATOM 541 CA THR 227
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                               55.856 44.150 17.326 1.00 22.41
           542 CB THR 227
     ATOM
     ATOM 543 OG1 THR 227
                                55.670 45.053 18.420 1.00 25.09
     ATOM 544 CG2 THR 227
                                54.558 44.041 16.560 1.00 24.29
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     ATOM 545 C THR 227
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     ATOM 548 CA ARG 228
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                                59.032 41.136 14.191 1.00 19.95
     ATOM 549 CB ARG 228
                                58.810 42.349 13.286 1.00 23.31
     ATOM 550 CG ARG 228
                                60.001 42.646 12.405 1.00 25.64
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     ATOM
           551 CD ARG 228
                                61.139 43.138 13.171 1.00 27.01
           552 NE ARG 228
     ATOM
                                62.209 42.413 13.468 1.00 28.20
     ATOM 553 CZ ARG 228
                                62.280 41.155 13.067 1.00 28.99
     ATOM 554 NH1 ARG 228
                                63.219 42.951 14.141 1.00 27.25
     ATOM 555 NH2 ARG 228
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     ATOM 556 C ARG 228
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57.433 38.431 14.788 1.00 17.50
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                               58.278 39.162 16.747 1.00 17.42
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            558 N VAL 229
            559 CA VAL 229
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    ATOM 560 CB VAL 229
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                                58.955 36.422 19.334 1.00 16.19
           561 CG1 VAL 229
    ATOM
                                60.591 38.010 18.421 1.00 14.44
    ATOM
           562 CG2 VAL 229
    ATOM 563 C VAL 229
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           564 O VAL 229
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            565 N VAL 230
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           566 CA VAL 230
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                               53.896 39.327 18.897 1.00 18.60
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            568 CG1 VAL 230
                                54.445 39.629 20.299 1.00 17.82
            569 CG2 VAL 230
    ATOM
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           570 C VAL 230
                              53.938 37.780 16.916 1.00 18.46
                               53.115 36.863 16.828 1.00 18.46
            571 O VAL 230
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           572 N ASP 231
                              54.289 38.539 15.874 1.00 19.21
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    ATOM 573 CA ASP 231
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           574 CB ASP 231
                               54.231 39.415 13.555 1.00 20.98
            575 CG ASP 231
                               53.754 40.817 13.915 1.00 24.11
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            576 OD1 ASP 231
                               52.704 40.953 14.586 1.00 24.23
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    ATOM
                                54.443 41.784 13.522 1.00 25.90
    ATOM
           577 OD2 ASP 231
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    ATOM
            578 C ASP 231
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           579 O ASP 231
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            582 CB PHE 232
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    ATOM
            583 CG PHE 232
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            584 CD1 PHE 232
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            586 CE1 PHE 232
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    ATOM
           588 CZ PHE 232
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            593 CB ALA 233
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    ATOM 594 C ALA 233
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           595 O ALA 233
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            599 CG LYS 234
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            602 NZ LYS 234
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            604 O LYS 234
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52.350 33.791 10.819 1.00 25.23
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            608 CG LYS 235
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            609 CD LYS 235
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            610 CE LYS 235
            611 NZ LYS 235
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     ATOM
     ATOM
            612 C LYS 235
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     ATOM 613 O LYS 235
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     ATOM
     ATOM 616 CB LEU 236
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     ATOM 617 CG LEU 236
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            618 CD1 LEU 236
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     ATOM 619 CD2 LEU 236
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            621 O LEU 236
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            622 N PRO 237
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                               50.829 27.156 11.668 1.00 35.04
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     ATOM 624 CA PRO 237
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            625 CB PRO 237
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     ATOM 626 CG PRO 237
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     ATOM 627 C PRO 237
                              48.582 26.720 14.447 1.00 37.82
     ATOM 628 O PRO 237
                              47.629 27.102 15.125 1.00 37.08
            629 N MET 238
                               49.495 25.893 14.935 1.00 40.42
     ATOM
     ATOM 630 CA MET 238
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            631 CB MET 238
                               50.453 24.298 16.549 1.00 45.20
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            632 CG MET 238
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            636 O MET 238
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     ATOM
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     ATOM
            640 CG PHE 239
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     ATOM 641 CD1 PHE 239
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     ATOM 644 CE2 PHE 239
     ATOM 645 CZ PHE 239
                               51.726 32.612 20.761 1.00 24.52
                              48.574 29.582 18.352 1.00 36.84
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     ATOM 646 C PHE 239
     ATOM 647 O PHE 239
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            648 N SER 240
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     ATOM 649 CA SER 240
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     ATOM 650 CB SER 240
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     ATOM 651 C SER 240
                              45.627 30.304 17.981 1.00 37.30
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    ATOM
            652 O SER 240
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                               45.639 28.974 17.917 1.00 37.73
     ATOM
            653 N GLU 241
     ATOM 654 CA GLU 241
                               44.531 28.155 18.418 1.00 38.44
     ATOM 655 CB GLU 241
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                               44.290 26.471 16.436 1.00 48.01
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	ATOM	658 OE1 GLU 241	44.375 24.088 16.779 1.00 51.14
	ATOM	659 OE2 GLU 241	44.957 24.838 14.799 1.00 50.68
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	ATOM	662 N LEU 242	45.762 28.329 20.480 1.00 33.28
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	ATOM	665 CG LEU 242	48.318 27.202 21.797 1.00 29.95
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	ATOM	667 CD2 LEU 242	47.935 25.931 22.564 1.00 29.57
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	ATOM	698 C ASP 246	50.065 30.983 25.826 1.00 23.57
	ATOM	699 O ASP 246	51.288 30.993 25.955 1.00 22.61
	ATOM	700 N GLN 247	49.431 31.630 24.852 1.00 23.23
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	ATOM	703 CG GLN 247	48.329 32.307 22.066 1.00 22.74
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	ATOM	708 O GLN 247	52.280 33.454 24.182 1.00 23.07
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5	ATOM	711 CB ILE 248	50.473 35.824 27.273 1.00 24.59
-	ATOM	712 CG2 ILE 248	51.304 36.682 28.242 1.00 24.09
	ATOM	713 CG1 ILE 248	49.499 36.707 26.487 1.00 23.47
	ATOM	714 CD1 ILE 248	48.413 37.323 27.341 1.00 23.84
	ATOM	715 C ILE 248	52.568 34.387 26.986 1.00 22.27
10	ATOM	716 O ILE 248	53.705 34.833 26.829 1.00 22.06
	ATOM	717 N ILE 249	52.321 33.313 27.729 1.00 21.40
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	ATOM	719 CB ILE 249	52.850 31.438 29.279 1.00 23.53
	ATOM	720 CG2 ILE 249	53.972 30.489 29.711 1.00 21.44
15	ATOM	721 CG1 ILE 249	52.098 31.963 30.500 1.00 22.76
	ATOM	722 CD1 ILE 249	51.252 30.911 31.175 1.00 25.03
	ATOM	723 C ILE 249	54.481 32.148 27.470 1.00 22.24
	ATOM	724 O ILE 249	55.677 32.321 27.733 1.00 22.90
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	ATOM	730 CD2 LEU 250	54.494 28.050 25.386 1.00 18.52
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	ATOM	732 O LEU 250	57.069 32.094 24.603 1.00 20.27
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	ATOM	735 CB LEU 251	54.806 35.543 23.471 1.00 22.76
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	ATOM	738 CD2 LEU 251	53.040 35.708 21.747 1.00 22.86
	ATOM	739 C LEU 251	56.891 35.030 24.776 1.00 23.67
	ATOM	740 O LEU 251	58.051 35.234 24.402 1.00 22.58
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	ATOM	742 CA LYS 252	57.395 35.754 27.057 1.00 26.22
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	ATOM	747 NZ LYS 252	54.477 38.870 31.168 1.00 44.60
	ATOM	748 C LYS 252	58.566 34.793 27.312 1.00 25.26
	ATOM	749 O LYS 252	59.701 35.222 27.555 1.00 26.67
	ATOM	750 N GLY 253	58.306 33.497 27.195 1.00 23.97
45	ATOM	751 CA GLY 253	59.356 32.521 27.404 1.00 22.00
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_	ATOM	762 CB CYS 255	60,292 37.407 23.634 1.00 21.21
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10	ATOM	767 CA MET 256	64.657 36.874 23.835 1.00 20.07
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	ATOM	769 CG MET 256	66.744 37.360 25.267 1.00 19.20
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15	ATOM	771 CE MET 256	68.856 38.971 24.375 1.00 18.47
13	ATOM	771 CE MET 256	65.408 35.830 23.005 1.00 18.75
	ATOM	772 C MET 256	66.305 36.164 22.225 1.00 18.15
	ATOM	773 O ML1 250 774 N GLU 257	65.035 34.568 23.170 1.00 19.00
	ATOM	774 N GEO 237 775 CA GLU 257	65.685 33.480 22.443 1.00 19.71
20	ATOM	776 CB GLU 257	65.104 32.145 22.882 1.00 21.15
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	ATOM	777 CG GLU 257	64.513 30.820 24.929 1.00 30.75
	ATOM	778 CB GLU 257	63.875 30.069 24.162 1.00 32.36
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23	ATOM	781 C GLU 257	66.521 33.506 20.197 1.00 17.58
	ATOM	783 N ILE 258	64.336 33.977 20.497 1.00 17.78
	ATOM	784 CA ILE 258	64.101 34.176 19.081 1.00 17.60
	ATOM	785 CB ILE 258	62.590 34.267 18.765 1.00 16.35
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30	ATOM	787 CG1 ILE 258	61.935 32.884 18.980 1.00 17.24
	ATOM	788 CD1 ILE 258	60.437 32.787 18.593 1.00 14.08
	ATOM	789 C ILE 258	64.872 35.408 18.595 1.00 19.11
	ATOM	790 O ILE 258	65.609 35.326 17.601 1.00 19.02
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	ATOM	795 SD MET 259	63.452 40.921 20.700 1.00 24.33
40	ATOM	796 CE MET 259	63.769 40.595 22.415 1.00 22.50
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	ATOM	797 C MET 259	67.638 37.993 17.941 1.00 19.96
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15			69.387 35.840 21.195 1.00 17.25
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	ATOM	810 CD2 LEU 261	66.470 31.060 15.937 1.00 13.72
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-	ATOM	812 O LEU 261	69.766 34.619 15.194 1.00 16.68
	ATOM	813 N ARG 262	67.848 35.620 15.853 1.00 16.47
	ATOM	814 CA ARG 262	67.778 36.493 14.680 1.00 16.66
	ATOM	815 CB ARG 262	66.475 37.279 14.693 1.00 16.00
10	ATOM	816 CG ARG 262	65.291 36.404 14.354 1.00 15.62
- •	ATOM	817 CD ARG 262	63.995 37.167 14.378 1.00 17.31
	ATOM	818 NE ARG 262	62.967 36.454 13.628 1.00 20.09
	ATOM	819 CZ ARG 262	61.755 36.932 13.361 1.00 21.06
	ATOM	820 NH1 ARG 262	61.390 38.136 13.787 1.00 19.02
15	ATOM	821 NH2 ARG 262	60.909 36.207 12.640 1.00 22.63
	ATOM	822 C ARG 262	69.003 37.396 14.527 1.00 16.80
	ATOM	823 O ARG 262	69.440 37.664 13.412 1.00 16.82
	ATOM	824 N ALA 263	69.578 37.832 15.650 1.00 17.77
	ATOM	825 CA ALA 263	70.795 38.647 15.637 1.00 18.41
20	ATOM	826 CB ALA 263	70.996 39.337 17.004 1.00 18.26
_ •	ATOM	827 C ALA 263	71.998 37.740 15.327 1.00 19.15
	ATOM	828 O ALA 263	72.837 38.063 14.475 1.00 19.40
	ATOM	829 N ALA 264	72.056 36.587 15.996 1.00 19.84
	ATOM	830 CA ALA 264	73.155 35.633 15.818 1.00 20.35
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	ATOM	832 C ALA 264	73.289 35.079 14.398 1.00 20.66
	ATOM	833 O ALA 264	74.406 34.870 13.922 1.00 21.04
	ATOM	834 N VAL 265	72.173 34.822 13.723 1.00 21.14
	ATOM	835 CA VAL 265	72.249 34.299 12.358 1.00 22.96
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	ATOM	837 CG1 VAL 265	70.458 32.600 12.866 1.00 19.48
	ATOM	838 CG2 VAL 265	69.838 34.708 11.698 1.00 18.96
	ATOM	839 C VAL 265	72.718 35.387 11.382 1.00 24.66
	ATOM	840 O VAL 265	73.026 35.103 10.224 1.00 26.03
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	ATOM	843 CB ARG 266	72.187 38.819 10.964 1.00 24.09
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	ATOM	845 CD ARG 266	69.998 39.492 10.098 1.00 24.80
40	ATOM	846 NE ARG 266	68.961 39.253 9.109 1.00 24.01
	ATOM	847 CZ ARG 266	67.833 39.940 9.069 1.00 23.26
	ATOM	848 NH1 ARG 266	67.613 40.880 9.970 1.00 24.16
	ATOM	849 NH2 ARG 266	66.960 39.733 8.099 1.00 23.31
	ATOM	850 C ARG 266	74.543 38.273 11.543 1.00 28.07
45	ATOM	851 O ARG 266	74.786 39.479 11.517 1.00 29.67
	ATOM	852 N TYR 267	75.367 37.366 12.053 1.00 28.90
	ATOM	853 CA TYR 267	76.679 37.714 12.558 1.00 30.23
	ATOM	854 CB TYR 267	77.223 36.584 13.434 1.00 29.98
	ATOM	855 CG TYR 267	78.699 36.702 13.727 1.00 31.75
50	ATOM	856 CD1 TYR 267	79.179 37.577 14.712 1.00 31.21

	ATOM	857 CEI TYR 267	80.544 37.705 14.950 1.00 31.29
	ATOM	858 CD2 TYR 267	79.625 35.958 12.994 1.00 31.84
	ATOM	859 CE2 TYR 267	80.986 36.078 13.222 1.00 32.15
	ATOM	860 CZ TYR 267	81.442 36.949 14.197 1.00 32.60
5	ATOM	861 OH TYR 267	82.801 37.052 14.389 1.00 34.13
	ATOM	862 C TYR 267	77.570 37.900 11.343 1.00 31.17
	ATOM	863 O TYR 267	77.543 37.086 10.426 1.00 30.91
	ATOM	864 N ASP 268	78.361 38.966 11.336 1.00 33.09
	ATOM	865 CA ASP 268	79.252 39.233 10.216 1.00 35.57
10	ATOM	866 CB ASP 268	79.085 40.679 9.747 1.00 39.39
	ATOM	867 CG ASP 268	79.796 40.954 8.432 1.00 42.22
	ATOM	868 OD1 ASP 268	79.426 40.331 7.412 1.00 46.07
	ATOM	·869 OD2 ASP 268	80.718 41.798 8.415 1.00 44.30
	ATOM	870 C ASP 268	80.700 38.967 10.620 1.00 35.72
15	ATOM	871 O ASP 268	81.287 39.737 11.384 1.00 34.49
	ATOM	872 N PRO 269	81.295 37.872 10.108 1.00 37.00
	ATOM	873 CD PRO 269	80.712 36.887 9.182 1.00 36.77
	ATOM	874 CA PRO 269	82.679 37.514 10.427 1.00 38.52
	ATOM	875 CB PRO 269	82.905 36.239 9.611 1.00 37.06
20	ATOM	876 CG PRO 269	81.549 35.669 9.453 1.00 36.19
	ATOM	877 C PRO 269	83.656 38.613 10.019 1.00 40.96
	ATOM	878 O PRO 269	84.586 38.929 10.760 1.00 42.23
	ATOM	879 N ALA 270	83.418 39.209 8.854 1.00 41.92
	ATOM	880 CA ALA 270	84.277 40.272 8.342 1.00 42.08
25	ATOM	881 CB ALA 270	83.709 40.838 7.029 1.00 42.64
	ATOM	882 C ALA 270	84.495 41.394 9.355 1.00 41.70
	ATOM	883 O ALA 270	85.632 41.709 9.684 1.00 42.25
	ATOM	884 N SER 271	83.408 41.970 9.865 1.00 41.87
	ATOM	885 CA SER 271	83.495 43.073 10.830 1.00 40.75
30	ATOM	886 CB SER 271	82.454 44.143 10.500 1.00 40.60
	ATOM	887 OG SER 271	81.150 43.590 10.464 1.00 40.31
	ATOM	888 C SER 271	83.344 42.658 12.290 1.00 39.99
	ATOM	889 O SER 271	83.484 43.487 13.194 1.00 38.77
	ATOM	890 N ASP 272	83.042 41.381 12.508 1.00 38.94
35	ATOM	891 CA ASP 272	82.859 40.844 13.845 1.00 37.78
	ATOM	892 CB ASP 272	84.182 40.904 14.625 1.00 38.86
	ATOM	893 CG ASP 272	84.094 40.255 16.000 1.00 41.09
	ATOM	894 OD1 ASP 272	83.342 39.275 16.173 1.00 41.64
40	ATOM	895 OD2 ASP 272	84.781 40.734 16.924 1.00 43.84
40	ATOM	896 C ASP 272	81.744 41.634 14.536 1.00 36.92
	ATOM	897 O ASP 272	81.907 42.156 15.648 1.00 37.56
	ATOM	898 N THR 273	80.603 41.723 13.865 1.00 33.65
	ATOM	899 CA THR 273	79.469 42.443 14.425 1.00 31.57
	ATOM	900 CB THR 273	79.246 43.790 13.695 1.00 31.69
45	ATOM	901 OG1 THR 273	79.087 43.557 12.289 1.00 30.71
	ATOM	902 CG2 THR 273	80.426 44.730 13.922 1.00 31.53
	ATOM	903 C THR 273	78.184 41.631 14.310 1.00 30.15
	ATOM	904 O THR 273	78.104 40.697 13.504 1.00 30.10
50	ATOM	905 N LEU 274	77.213 41.942 15.164 1.00 27.09
50	ATOM	906 CA LEU 274	75.907 41.303 15.103 1.00 25.94

	ATOM ATOM	907 CB LEU 274 908 CG LEU 274	75.396 40.936 16.496 1.00 24.47 76.020 39.731 17.206 1.00 23.33
	ATOM	909 CD1 LEU 274	75.436 39.631 18.602 1.00 21.14
	ATOM	910 CD2 LEU 274	75.792 38.444 16.427 1.00 20.04
5	ATOM	911 C LEU 274	75.010 42.377 14.500 1.00 26.57
,	ATOM	912 O LEU 274	75.339 43.557 14.568 1.00 27.03
	ATOM	913 N THR 275	73.914 41.987 13.865 1.00 26.60
	ATOM	914 CA THR 275	73.009 42.966 13.285 1.00 26.48
	ATOM	915 CB THR 275	72.786 42.717 11.781 1.00 26.52
10	ATOM	916 OG1 THR 275	74.044 42.719 11.097 1.00 28.67
•	ATOM	917 CG2 THR 275	71.919 43.799 11.198 1.00 27.35
	ATOM	918 C THR 275	71.674 42.898 14.014 1.00 26.57
	ATOM	919 O THR 275	71.069 41.825 14.121 1.00 28.50
	ATOM	920 N LEU 276	71.236 44.026 14.564 1.00 25.18
15	ATOM	921 CA LEU 276	69,970 44.069 15.276 1.00 24.61
	ATOM	922 CB LEU 276	70.057 44.987 16.506 1.00 23.61
	ATOM	923 CG LEU 276	71.199 44.730 17.503 1.00 24.36
	ATOM	924 CD1 LEU 276	71.039 45.654 18.709 1.00 19.91
	ATOM	925 CD2 LEU 276	71.225 43.253 17.947 1.00 22.20
20	ATOM	926 C LEU 276	68.894 44.560 14.322 1.00 25.63
	ATOM	927 O LEU 276	69.100 45.556 13.623 1.00 25.35
	ATOM	928 N SER 277	67.787 43.814 14.249 1.00 25.94
	ATOM	929 CA SER 277	66.634 44.141 13.403 1.00 24.61
	ATOM	930 CB SER 277	65.874 45.335 13.987 1.00 21.96
25	ATOM	931 OG SER 277	65.368 45.029 15.273 1.00 19.68
	ATOM	932 C SER 277	67.005 44.406 11.946 1.00 25.20
	ATOM	933 O SER 277	66.350 45.199 11.267 1.00 25.21
	ATOM	934 N GLY 278	68.067 43.747 11.489 1.00 27.08
	ATOM	935 CA GLY 278	68.556 43.899 10.127 1.00 29.27
30	ATOM	936 C GLY 278	69.022 45.297 9.753 1.00 31.57
	ATOM	937 O GLY 278	69.303 45.564 8.591 1.00 31.42
	ATOM	938 N GLU 279	69.159 46.177 10.740 1.00 33.41
	ATOM	939 CA GLU 279	69.558 47.560 10.484 1.00 34.84
2.5	ATOM	940 CB GLU 279	68.345 48.485 10.650 1.00 36.16
35	ATOM	941 CG GLU 279	67.843 48.606 12.090 1.00 38.08 66.566 49.419 12.206 1.00 41.07
	ATOM	942 CD GLU 279 943 OE1 GLU 279	66.475 50.279 13.108 1.00 41.98
	ATOM		65.643 49.197 11.399 1.00 43.80
	ATOM	944 OE2 GLU 279 945 C GLU 279	70.706 48.116 11.326 1.00 34.38
40	ATOM	945 C GLU 279 946 O GLU 279	71.366 49.057 10.901 1.00 35.60
40	ATOM	946 O GLU 279 947 N MET 280	70.944 47.565 12.511 1.00 33.43
	ATOM ATOM	947 N MET 280 948 CA MET 280	72.014 48.085 13.358 1.00 32.27
	ATOM	949 CB MET 280	71.443 48.544 14.702 1.00 31.81
	ATOM	950 CG MET 280	72.471 49.181 15.637 1.00 29.76
45	ATOM	951 SD MET 280	71.813 49.482 17.289 1.00 29.63
43	ATOM	951 SD MET 280 952 CE MET 280	70.592 50.735 16.989 1.00 24.91
	ATOM	952 CE MET 280	73.161 47.119 13.603 1.00 32.51
	ATOM	954 O MET 280	72.995 46.117 14.303 1.00 32.78
	ATOM	955 N ALA 281	74.321 47.408 13.021 1.00 31.74
50	ATOM	956 CA ALA 281	75.491 46.564 13.231 1.00 32.25
50	AT OW	750 CA ALA 201	,5.471 10.501 15.551 1.00 52.25

	ATOM	957 CB ALA 281	76.494 46.740 12.108 1.00 30.91
	ATOM	958 C ALA 281	76.091 47.006 14.563 1.00 33.09
	ATOM	959 O ALA 281	76.261 48.202 14.805 1.00 34.06
	ATOM	960 N VAL 282	76.358 46.053 15.447 1.00 33.78
5	ATOM	961 CA VAL 282	76.913 46.366 16.755 1.00 33.45
	ATOM	962 CB VAL 282	75.858 46.208 17.885 1.00 34.92
	ATOM	963 CG1 VAL 282	74.775 47.269 17.744 1.00 34.90
	ATOM	964 CG2 VAL 282	75.246 44.806 17.860 1.00 34.39
	ATOM	965 C VAL 282	78.119 45.514 17.087 1.00 33.93
10	ATOM	966 O VAL 282	78.202 44.347 16.702 1.00 35.11
	ATOM	967 N LYS 283	79.071 46.123 17.777 1.00 33.49
	ATOM	968 CA LYS 283	80.285 45.446 18.187 1.00 34.83
	ATOM	969 CB LYS 283	81.446 46.445 18.183 1.00 35.96
	ATOM	970 CG LYS 283	81.726 47.013 16.797 1.00 39.20
15	ATOM	971 CD LYS 283	82.621 48.245 16.844 1.00 43.38
	ATOM	972 CE LYS 283	83.142 48.611 15.455 1.00 44.17
	ATOM	973 NZ LYS 283	84.077 47.563 14.922 1.00 47.27
	ATOM	974 C LYS 283	80.068 44.832 19.572 1.00 33.94
	ATOM	975 O LYS 283	79.134 45.215 20.290 1.00 33.85
20	ATOM	976 N ARG 284	80.939 43.895 19.941 1.00 33.63
	ATOM	977 CA ARG 284	80.873 43.184 21.217 1.00 34.00
	ATOM	978 CB ARG 284	82.094 42.285 21.381 1.00 34.04
	ATOM	979 CG ARG 284	82.332 41.369 20.219 1.00 36.31
	ATOM	980 CD ARG 284	83.638 40.643 20.354 1.00 37.03
25	ATOM	981 NE ARG 284	83.724 39.576 19.369 1.00 39.27
	ATOM	982 CZ ARG 284	83.323 38.326 19.583 1.00 40.07
	ATOM	983 NH1 ARG 284	82.804 37.973 20.759 1.00 39.78
	ATOM	984 NH2 ARG 284	83.434 37.428 18.613 1.00 40.16
	ATOM	985 C ARG 284	80.787 44.101 22.419 1.00 35.16
30	ATOM	986 O ARG 284	79.884 43.977 23.249 1.00 35.87
	ATOM	987 N GLU 285	81.763 44.993 22.530 1.00 35.75
	ATOM	988 CA GLU 285	81.827 45.939 23.632 1.00 36.86
	ATOM	989 CB GLU 285	83.071 46.818 23.464 1.00 40.47
	ATOM	990 CG GLU 285	83.202 47.973 24.444 1.00 49.23
35	ATOM	991 CD GLU 285	83.587 49.284 23.747 1.00 54.22
	ATOM	992 OE1 GLU 285	84.784 49.657 23.760 1.00 55.37
	ATOM	993 OE2 GLU 285	82.686 49.942 23.176 1.00 56.95
	ATOM	994 C GLU 285	80.552 46.785 23.684 1.00 34.45
	ATOM	995 O GLU 285	79.990 47.007 24.754 1.00 34.47
40	ATOM	996 N GLN 286	80.046 47.166 22.515 1.00 32.27
	ATOM	997 CA GLN 286	78.853 47.991 22.438 1.00 30.35
	ATOM	998 CB GLN 286	78.615 48.472 21.006 1.00 33.34
	ATOM	999 CG GLN 286	79.632 49.497 20.500 1.00 35.09
	ATOM	1000 CD GLN 286	79.293 50.023 19.108 1.00 38.42
45	ATOM	1001 OE1 GLN 286	79.161 49.248 18.158 1.00 39.03
	ATOM	1002 NE2 GLN 286	
	ATOM	1003 C GLN 286	77.605 47.308 22.970 1.00 29.57
	ATOM	1004 O GLN 286	76.870 47.891 23.770 1.00 26.96
	ATOM	1005 N LEU 287	77.352 46.080 22.524 1.00 29.50
50	ATOM	1006 CA LEU 287	76.164 45.350 22.979 1.00 28.93

	ATOM	1007 CB LEU 287	75.831 44.182 22.029 1.00 27.14
	ATOM	1008 CG LEU 287	74.474 43.484 22.227 1.00 24.66
	ATOM	1009 CD1 LEU 287	73.316 44.475 22.184 1.00 22.70
	ATOM	1010 CD2 LEU 287	74.297 42.413 21.163 1.00 25.17
5	ATOM	1011 C LEU 287	76.303 44.874 24.433 1.00 28.10
_	ATOM	1012 O LEU 287	75.301 44.748 25.155 1.00 28.58
	ATOM	1013 N LYS 288	77.541 44.652 24.868 1.00 27.97
	ATOM	1014 CA LYS 288	77.808 44.218 26.230 1.00 28.55
	ATOM	1015 CB LYS 288	79.270 43.800 26.376 1.00 28.93
10	ATOM	1016 CG LYS 288	79.603 43.254 27.750 1.00 32.46
10	ATOM	1017 CD LYS 288	81.015 42.725 27.826 1.00 33.48
	ATOM	1018 CE LYS 288	81.205 41.878 29.071 1.00 35.76
	ATOM	1019 NZ LYS 288	82.525 41.186 29.029 1.00 40.52
	ATOM	1020 C LYS 288	77.497 45.341 27.220 1.00 29.15
15	ATOM	1021 O LYS 288	76.782 45.132 28.207 1.00 31.28
13	ATOM	1021 O L13 288	77.996 46.539 26.933 1.00 28.58
	ATOM	1023 CA ASN 289	77.794 47.692 27.811 1.00 28.40
	ATOM	1024 CB ASN 289	78.815 48.775 27.485 1.00 28.28
	ATOM	1024 CB ASN 289	80.224 48.329 27.770 1.00 31.30
20	ATOM	1026 OD1 ASN 289	80.445 47.442 28.601 1.00 33.02
20			81.190 48.928 27.087 1.00 30.49
	ATOM		76.395 48.278 27.792 1.00 30.49
	ATOM		76.393 48.278 27.792 1.00 28.33
	ATOM		
0.5	ATOM	1030 N GLY 290	75.638 47.977 26.740 1.00 26.71
25	ATOM	1031 CA GLY 290	74.286 48.487 26.606 1.00 23.27
	ATOM	1032 C GLY 290	73.233 47.852 27.484 1.00 22.93
	ATOM	1033 O GLY 290	72.063 48.219 27.399 1.00 23.84
	ATOM	1034 N GLY 291	73.620 46.905 28.330 1.00 21.30
•	ATOM	1035 CA GLY 291	72.637 46.290 29.199 1.00 20.38
30	ATOM	1036 C GLY 291	72.653 44.778 29.200 1.00 20.05
	ATOM	1037 O GLY 291	72.190 44.165 30.147 1.00 21.91
	ATOM	1038 N LEU 292	73.211 44.173 28.160 1.00 21.36
•	ATOM	1039 CA LEU 292	73.248 42.717 28.062 1.00 21.51
	ATOM	1040 CB LEU 292	73.319 42.280 26.593 1.00 18.52
35	ATOM	1041 CG LEU 292	72.019 42.506 25.815 1.00 17.07
	ATOM	1042 CD1 LEU 292	72.103 41.818 24.479 1.00 18.09
	ATOM	1043 CD2 LEU 292	70.844 41.947 26.599 1.00 16.35
			74.347 42.046 28.872 1.00 22.17
			74.176 40.923 29.352 1.00 21.91
40		1046 N GLY 293	
	ATOM		76.588 42.169 29.760 1.00 23.92
	ATOM	1048 C GLY 293	
	ATOM	1049 O GLY 293	
	ATOM		77.332 39.866 29.867 1.00 26.08
45	ATOM	1051 CA VAL 294	77.854 38.618 29.329 1.00 26.34
	ATOM	•	78.263 37.636 30.443 1.00 26.97
	ATOM	1053 CG1 VAL 294	79.440 38.199 31.209 1.00 28.20
	ATOM		77.099 37.371 31.384 1.00 25.56
	ATOM		
50	ATOM	1056 O VAL 294	77.315 37.097 27.568 1.00 27.65

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75.608 38.304 28.408 1.00 26.09
     ATOM 1057 N VAL 295
     ATOM 1058 CA VAL 295
                                74.606 37.740 27.499 1.00 26.65
     ATOM 1059 CB VAL 295
                                73.186 38.312 27.777 1.00 28.39
                                72.164 37.740 26.782 1.00 26.69
     ATOM 1060 CG1 VAL 295
                                 72.763 38.005 29.206 1.00 26.23
    ATOM 1061 CG2 VAL 295
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     ATOM 1062 C VAL 295
     ATOM 1063 O VAL 295
                               74.903 37.286 25.151 1.00 27.12
                               75.609 39.275 25.908 1.00 24.95
     ATOM 1064 N SER 296
     ATOM 1065 CA SER 296
                               76.097 39.725 24.619 1.00 26.17
                               76.665 41.132 24.742 1.00 25.82
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    ATOM 1066 CB SER 296
                                77.253 41.554 23.525 1.00 26.64
    ATOM 1067 OG SER 296
     ATOM 1068 C SER 296
                               77.196 38.783 24.142 1.00 28.63
                               77.241 38.420 22.963 1.00 29.19
     ATOM 1069 O SER 296
    ATOM 1070 N ASP 297
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    ATOM 1071 CA ASP 297
                               79.211 37.531 24.731 1.00 28.96
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                               80.058 37.234 25.973 1.00 31.82
     ATOM 1072 CB ASP 297
    ATOM 1073 CG ASP 297
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    ATOM 1074 OD1 ASP 297
                                80.958 39.429 25.743 1.00 35.71
    ATOM 1075 OD2 ASP 297
                                81.140 38.430 27.698 1.00 37.68
                               78.605 36.227 24.247 1.00 27.63
    ATOM 1076 C ASP 297
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                               79.048 35.666 23.248 1.00 29.88
     ATOM 1077 O ASP 297
     ATOM 1078 N ALA 298
                               77.581 35.762 24.952 1.00 25.15
     ATOM 1079 CA ALA 298
                                76.909 34.527 24.592 1.00 24.49
                                75.811 34.224 25.594 1.00 21.91
     ATOM 1080 CB ALA 298
                               76.343 34.569 23.158 1.00 24.93
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    ATOM 1081 C ALA 298
                               76.589 33.654 22.357 1.00 24.83
     ATOM 1082 O ALA 298
    ATOM 1083 N ILE 299
                              75.632 35.647 22.814 1.00 24.70
                               75.041 35.756 21.480 1.00 22.49
     ATOM 1084 CA ILE 299
                               74.057 36.950 21.351 1.00 21.96
     ATOM 1085 CB ILE 299
                               73.338 36.876 20.005 1.00 19.17
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    ATOM 1086 CG2 ILE 299
                               72.994 36.876 22.459 1.00 21.16
     ATOM 1087 CG1 ILE 299
     ATOM 1088 CD1 ILE 299
                               72.363 38.228 22.853 1.00 22.04
     ATOM 1089 C ILE 299
                              76.127 35.829 20.428 1.00 22.33
                              75.995 35.234 19.367 1.00 24.80
    ATOM 1090 O ILE 299
                               77.209 36.538 20.724 1.00 21.92
    ATOM 1091 N PHE 300
35
                                78.322 36.641 19.785 1.00 23.08
     ATOM 1092 CA PHE 300
                                79.385 37.636 20.278 1.00 24.08
    ATOM 1093 CB PHE 300
                                79.249 39.017 19.686 1.00 24.18
     ATOM 1094 CG PHE 300
    ATOM 1095 CD1 PHE 300
                                78.494 39.991 20.325 1.00 22.64
                                79.857 39.331 18.471 1.00 23.76
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    ATOM 1096 CD2 PHE 300
     ATOM 1097 CE1 PHE 300
                                78.347 41.253 19.770 1.00 22.38
                                79.715 40.596 17.904 1.00 23.21
    ATOM 1098 CE2 PHE 300
                               78.957 41.558 18.554 1.00 22.46
    ATOM 1099 CZ PHE 300
                               78.948 35.274 19.561 1.00 23.06
    ATOM 1100 C PHE 300
                               79.264 34.913 18.426 1.00 23.97
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    ATOM 1101 O PHE 300
                               79.113 34.506 20.636 1.00 23.75
     ATOM 1102 N GLU 301
                                79.694 33.169 20.525 1.00 24.16
     ATOM 1103 CA GLU 301
     ATOM 1104 CB GLU 301
                                79.884 32.545 21.902 1.00 23.03
     ATOM 1105 C GLU 301
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                               79.240 31.591 18.777 1.00 25.11
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     ATOM 1106 O GLU 301
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	ATOM	1107 N LEU 302	77.472 32.394 19.926 1.00 23.12
	ATOM	1108 CA LEU 302	76.495 31.624 19.166 1.00 23.56
	ATOM	1109 CB LEU 302	75.082 31.865 19.701 1.00 21.75
	ATOM	1110 CG LEU 302	73.953 31.120 18.979 1.00 22.61
5	ATOM	1111 CD1 LEU 302	74.084 29.612 19.193 1.00 22.31
	ATOM	1112 CD2 LEU 302	72.611 31.604 19.485 1.00 19.27
	ATOM	1113 C LEU 302	76.588 32.011 17.687 1.00 24.41
	ATOM	1114 O LEU 302	76.670 31.140 16.814 1.00 24.63
	ATOM	1115 N GLY 303	76.651 33.316 17.425 1.00 25.69
10	ATOM	1116 CA GLY 303	76.746 33.816 16.062 1.00 25.87
	ATOM	1117 C GLY 303	77.975 33.288 15.338 1.00 28.63
	ATOM	1118 O GLY 303	77.893 32.895 14.170 1.00 28.30
	ATOM	1119 N LYS 304	79.116 33.279 16.023 1.00 29.53
	ATOM	1120 CA LYS 304	80.360 32.791 15.437 1.00 31.18
15	ATOM	1121 CB LYS 304	81.529 32.931 16.418 1.00 34.79
	ATOM	1122 CG LYS 304	82.157 34.307 16.506 1.00 40.28
	ATOM	1123 CD LYS 304	83.441 34.262 17.332 1.00 44.37
•	ATOM	1124 CE LYS 304	83.174 33.814 18.775 1.00 47.63
	ATOM	1125 NZ LYS 304	82.459 34.847 19.592 1.00 48.83
20	ATOM	1126 C LYS 304	80.245 31.328 15.042 1.00 30.87
	ATOM	1127 O LYS 304	80.632 30.944 13.932 1.00 29.53
	ATOM	1128 N SER 305	79.720 30.518 15.961 1.00 30.46
	ATOM	1129 CA SER 305	79.566 29.086 15.731 1.00 31.09
	ATOM	1130 CB SER 305	79.243 28.370 17.041 1.00 29.83
25	ATOM	1131 OG SER 305	77.990 28.783 17.550 1.00 34.66
	ATOM	1132 C SER 305	78.532 28.732 14.653 1.00 31.06
	ATOM	1133 O SER 305	78.745 27.799 13.872 1.00 31.84
	ATOM	1134 N LEU 306	77.436 29.491 14.594 1.00 29.43
	ATOM	1135 CA LEU 306	76.378 29.258 13.611 1.00 28.39
30	ATOM	1136 CB LEU 306	75.121 30.055 13.962 1.00 26.05
	ATOM	1137 CG LEU 306	74.306 29.573 15.157 1.00 26.33
	ATOM	1138 CD1 LEU 306	73.061 30.430 15.285 1.00 26.22 73.924 28.110 14.985 1.00 25.86
	ATOM	1139 CD2 LEU 306	76.754 29.529 12.157 1.00 28.66
25	ATOM	1140 C LEU 306	76.116 29.001 11.253 1.00 28.58
35	ATOM	1141 O LEU 306 1142 N SER 307	77.786 30.338 11.931 1.00 29.72
٠	ATOM	1142 N SER 307 1143 CA SER 307	78.224 30.667 10.577 1.00 31.19
	ATOM	1144 CB SER 307	79.466 31.556 10.617 1.00 30.15
	ATOM ATOM	1145 OG SER 307	79.226 32.710 11.396 1.00 35.19
40	ATOM	1146 C SER 307	78.531 29.412 9.777 1.00 32.75
40	ATOM	1147 O SER 307	78.110 29.283 8.621 1.00 33.09
	ATOM	1148 N ALA 308	79.248 28.482 10.407 1.00 33.36
	ATOM	1148 N ALA 308	79.626 27.223 9.769 1.00 34.50
	ATOM	1150 CB ALA 308	80.636 26.473 10.637 1.00 33.55
45	ATOM	1151 C ALA 308	78.417 26.328 9.466 1.00 35.00
43	ATOM	1151 C ALA 300 1152 O ALA 308	78.469 25.501 8.550 1.00 37.10
	ATOM	1152 O ALA 308 1153 N PHE 309	77.335 26.496 10.226 1.00 32.76
	ATOM	1154 CA PHE 309	76.134 25.698 10.028 1.00 31.73
	ATOM	1155 CB PHE 309	75.214 25.818 11.232 1.00 30.04
50	ATOM	1156 CG PHE 309	75.705 25.091 12.438 1.00 31.19
50		1100 00 1110 507	

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ATOM 1157 CD1 PHE 309
                                74.973 24.048 12.975 1.00 31.61
                                76.884 25.459 13.054 1.00 31.92
    ATOM 1158 CD2 PHE 309
    ATOM 1159 CE1 PHE 309
                               75.400 23.391 14.110 1.00 31.22
                               77.320 24.807 14.194 1.00 31.01
    ATOM 1160 CE2 PHE 309
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    ATOM 1161 CZ PHE 309
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    ATOM 1162 C PHE 309
                              74.516 25.269 8.310 1.00 31.28
    ATOM 1163 O PHE 309
                               75.661 27.220 8.181 1.00 31.12
    ATOM 1164 N ASN 310
                               75.020 27.711 6.957 1.00 30.34
    ATOM 1165 CA ASN 310
                               75.636 27.036 5.719 1.00 31.63
    ATOM 1166 CB ASN 310
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    ATOM 1167 C ASN 310
                               73.511 27.492 7.003 1.00 29.40
    ATOM 1168 O ASN 310
                               72.939 26.791 6.156 1.00 29.15
    ATOM 1169 N LEU 311
                               72.875 28.055 8.026 1.00 27.60
                               71.435 27.907 8.205 1.00 28.23
    ATOM 1170 CA LEU 311
    ATOM 1171 CB LEU 311
                               71.021 28.313 9.621 1.00 27.41
15
    ATOM 1172 CG LEU 311
                               71.603 27.558 10.822 1.00 26.80
    ATOM 1173 CD1 LEU 311
                                70.949 28.078 12.112 1.00 25.05
                              71.360 26.062 10.662 1.00 24.72
    ATOM 1174 CD2 LEU 311
    ATOM 1175 C LEU 311
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    ATOM 1176 O LEU 311
    ATOM 1177 N ASP 312
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    ATOM 1178 CA ASP 312
    ATOM 1179 CB ASP 312
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                               67.438 26.890 4.754 1.00 21.34
    ATOM 1180 CG ASP 312
    ATOM 1181 OD1 ASP 312
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    ATOM 1182 OD2 ASP 312
                                67.154 26.206 3.758 1.00 22.18
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    ATOM 1183 C ASP 312
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    ATOM 1184 O ASP 312
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    ATOM 1185 N ASP 313
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    ATOM 1186 CA ASP 313
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                               64.557 31.486 5.385 1.00 24.99
    ATOM 1187 CB ASP 313
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    ATOM 1188 CG ASP 313
    ATOM 1189 OD1 ASP 313
                                66.036 33.334 5.778 1.00 30.34
                                64.936 33.306 3.897 1.00 30.41
    ATOM 1190 OD2 ASP 313
                              64.480 29.650 7.053 1.00 21.47
    ATOM 1191 C ASP 313
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                               63.853 29.917 8.082 1.00 21.76
    ATOM 1192 O ASP 313
                               64.407 28.474 6.435 1.00 19.16
    ATOM 1193 N THR 314
                                63.580 27.386 6.966 1.00 18.79
    ATOM 1194 CA THR 314
    ATOM 1195 CB THR 314
                               63.398 26.240 5.913 1.00 19.68
                                62.743 26.758 4.747 1.00 20.56
     ATOM 1196 OG1 THR 314
40
                                62.558 25.112 6.482 1.00 18.84
     ATOM 1197 CG2 THR 314
                               64.133 26.818 8.293 1.00 15.38
    ATOM 1198 C THR 314
     ATOM 1199 O THR 314
                               63.383 26.538 9.223 1.00 14.08
                               65.445 26.656 8.376 1.00 15.16
     ATOM 1200 N GLU 315
                                66.051 26.126 9.593 1.00 16.78
     ATOM 1201 CA GLU 315
45
                                67.513 25.785 9.340 1.00 14.29
     ATOM 1202 CB GLU 315
                                67.611 24.483 8.579 1.00 15.13
     ATOM 1203 CG GLU 315
                                68.910 24.291 7.872 1.00 15.90
     ATOM 1204 CD GLU 315
                                69.625 25.285 7.639 1.00 19.80
     ATOM 1205 OE1 GLU 315
                                69.211 23.129 7.527 1.00 19.34
50
     ATOM 1206 OE2 GLU 315
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65.872 27.119 10.736 1.00 17.27
    ATOM 1207 C GLU 315
    ATOM 1208 O GLU 315
                               65.457 26.742 11.836 1.00 17.46
                               66.081 28.399 10.440 1.00 17.12
    ATOM 1209 N VAL 316
                                65.897 29.441 11.446 1.00 16.92
    ATOM 1210 CA VAL 316
                                66.336 30.828 10.918 1.00 15.89
    ATOM 1211 CB VAL 316
                                66.062 31.921 11.962 1.00 14.60
    ATOM 1212 CG1 VAL 316
                                67.811 30.785 10.579 1.00 15.95
    ATOM 1213 CG2 VAL 316
                               64.430 29.472 11.869 1.00 17.32
    ATOM 1214 C VAL 316
                               64.131 29.582 13.055 1.00 18.11
    ATOM 1215 O VAL 316
                               63.515 29.324 10.905 1.00 17.42
    ATOM 1216 N ALA 317
10
                                62.076 29.342 11.195 1.00 16.21
    ATOM 1217 CA ALA 317
                                61.262 29.321 9.910 1.00 14.63
    ATOM 1218 CB ALA 317
                               61.656 28.181 12.079 1.00 16.84
    ATOM 1219 C ALA 317
                               60.904 28.359 13.036 1.00 16.08
    ATOM 1220 O ALA 317
                               62.146 26.990 11.759 1.00 17.27
    ATOM 1221 N LEU 318
15
                               61.783 25.804 12.526 1.00 17.88
    ATOM 1222 CA LEU 318
                               62.141 24.525 11.748 1.00 17.58
    ATOM 1223 CB LEU 318
                                61.331 24.333 10.439 1.00 16.87
    ATOM 1224 CG LEU 318
                                61.837 23.155 9.658 1.00 15.79
    ATOM 1225 CD1 LEU 318
                                59.860 24.149 10.728 1.00 14.08
    ATOM 1226 CD2 LEU 318
20
                               62.394 25.852 13.932 1.00 18.20
    ATOM 1227 C LEU 318
                               61.733 25.495 14.910 1.00 18.71
    ATOM 1228 O LEU 318
    ATOM 1229 N LEU 319
                               63.614 26.380 14.034 1.00 17.73
                                64.288 26.531 15.321 1.00 16.57
    ATOM 1230 CA LEU 319
                                65.689 27.105 15.107 1.00 18.81
    ATOM 1231 CB LEU 319
25
                                66,733 27.223 16.224 1.00 21.77
    ATOM 1232 CG LEU 319
    ATOM 1233 CD1 LEU 319
                                66.767 25.994 17.117 1.00 23.03
                                68.076 27.421 15.554 1.00 20.86
    ATOM 1234 CD2 LEU 319
                               63.433 27.471 16.160 1.00 16.07
     ATOM 1235 C LEU 319
                               63.134 27.183 17.319 1.00 16.40
     ATOM 1236 O LEU 319
30
                               62.948 28.546 15.545 1.00 13.91
     ATOM 1237 N GLN 320
                                62.101 29.490 16.253 1.00 13.86
     ATOM 1238 CA GLN 320
                                61.782 30.697 15.373 1.00 13.26
     ATOM 1239 CB GLN 320
                                62,994 31.553 15.080 1.00 12.17
     ATOM 1240 CG GLN 320
                                62.691 32.802 14.253 1.00 13.98
     ATOM 1241 CD GLN 320
35
                                63.597 33.568 13.950 1.00 15.61
     ATOM 1242 OE1 GLN 320
                                61.436 32.993 13.862 1.00 13.85
     ATOM 1243 NE2 GLN 320
                               60.813 28.832 16.746 1.00 14.52
     ATOM 1244 C GLN 320
                               60,367 29.087 17.864 1.00 15.12
     ATOM 1245 O GLN 320
                               60.211 27.982 15.924 1.00 14.21
     ATOM 1246 N ALA 321
40
                                58.976 27.298 16.309 1.00 15.04
     ATOM 1247 CA ALA 321
                                58.408 26.519 15.115 1.00 13.84
     ATOM 1248 CB ALA 321
                               59.217 26.349 17.487 1.00 15.98
     ATOM 1249 C ALA 321
                               58.358 26.197 18.355 1.00 15.12
     ATOM 1250 O ALA 321
                               60.373 25.687 17.488 1.00 16.63
45
     ATOM 1251 N VAL 322
                                60.720 24.757 18.557 1.00 18.74
     ATOM 1252 CA VAL 322
                                62.012 23.943 18.231 1.00 19.42
     ATOM 1253 CB VAL 322
                                 62.493 23.154 19.455 1.00 19.45
     ATOM 1254 CG1 VAL 322
                                 61.745 22.986 17.083 1.00 19.05
     ATOM 1255 CG2 VAL 322
                               60.910 25.556 19.833 1.00 18.42
     ATOM 1256 C VAL 322
50
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	ATOM	1257 O VAL 322	60.421 25.164 20.886 1.00 19.46
	ATOM	1258 N LEU 323	61.607 26.685 19.735 1.00 18.65
	ATOM	1259 CA LEU 323	61.836 27.543 20.894 1.00 18.49
	ATOM	1260 CB LEU 323	62.710 28.740 20.508 1.00 18.36
5	ATOM	1261 CG LEU 323	64.179 28.449 20.186 1.00 18.13
	ATOM	1262 CD1 LEU 323	64.829 29.669 19.585 1.00 17.37
	ATOM	1263 CD2 LEU 323	64.923 27.999 21.447 1.00 17.27
	ATOM	1264 C LEU 323	60.499 28.029 21.454 1.00 18.38
	ATOM	1265 O LEU 323	60.275 28.008 22.663 1.00 18.81
10	ATOM	1266 N LEU 324	59.595 28.406 20.557 1.00 18.67
	ATOM	1267 CA LEU 324	58.275 28.897 20.924 1.00 19.02
	ATOM	1268 CB LEU 324	57.564 29.467 19.685 1.00 17.78
	ATOM	1269 CG LEU 324	56.095 29.891 19.838 1.00 17.59
	ATOM	1270 CD1 LEU . 324	55.983 31.123 20.709 1.00 18.15
15	ATOM	1271 CD2 LEU 324	55.489 30.180 18.476 1.00 16.43
	ATOM	1272 C LEU 324	57.354 27.884 21.610 1.00 19.62
	ATOM	1273 O LEU 324	56.735 28.185 22.633 1.00 19.40
	ATOM	1274 N MET 325	57.224 26.701 21.029 1.00 21.14
	ATOM	1275 CA MET 325	56.330 25.680 21.585 1.00 24.06
20	ATOM	1276 CB MET 325	55.857 24.738 20.473 1.00 24.68
	ATOM	1277 CG MET 325	55.169 25.444 19.303 1.00 24.49
	ATOM	1278 SD MET 325	53.759 26.457 19.820 1.00 26.18
	ATOM	1279 CE MET 325	52.609 25.252 20.373 1.00 24.03
	ATOM	1280 C MET 325	56.996 24.887 22.705 1.00 26.15
25	ATOM	1281 O MET 325	57.021 23.664 22.693 1.00 25.68
	ATOM	1282 N SER 326	57.555 25.593 23.671 1.00 29.34
	ATOM	1283 CA SER 326	58.232 24.938 24.774 1.00 32.40
	ATOM	1284 CB SER 326	59.512 25.701 25.112 1.00 32.12
30	ATOM	1285 OG SER 326	60.127 25.173 26.272 1.00 36.86
30	ATOM	1286 C SER 326 1287 O SER 326	57.317 24.831 25.996 1.00 34.04 56.532 25.741 26.280 1.00 33.24
	ATOM		57.366 23.687 26.674 1.00 35.62
	ATOM	1288 N THR 327 1289 CA THR 327	56.560 23.486 27.867 1.00 36.88
	ATOM ATOM	1289 CA THR 327 1290 CB THR 327	55.938 22.085 27.907 1.00 36.58
35	ATOM	1291 OG1 THR 327	56.953 21.094 27.714 1.00 38.58
33	ATOM	1291 OG1 THR 327	54.883 21.938 26.826 1.00 37.73
	ATOM	1292 CG2 HIR 327	57.378 23.733 29.135 1.00 38.77
	ATOM	1294 O THR 327	56.921 23.438 30.240 1.00 39.53
	ATOM	1295 N ASP 328	
40	ATOM	1296 CA ASP 328	59.473 24.573 30.099 1.00 43.20
40	ATOM	1297 CB ASP 328	60.940 24.698 29.655 1.00 46.47
	ATOM	1298 CG ASP 328	61.618 23.346 29.439 1.00 51.94
	ATOM	1299 OD1 ASP 328	62.547 23.278 28.601 1.00 55.43
	ATOM	1300 OD2 ASP 328	61.251 22.354 30.111 1.00 54.77
45	ATOM	1301 C ASP 328	59.001 25.905 30.653 1.00 43.79
43	ATOM	1302 O ASP 328	59.755 26.877 30.709 1.00 45.91
	ATOM	1303 N ARG 329	57.724 25.967 30.995 1.00 43.55
	ATOM	1304 CA ARG 329	57.143 27.178 31.542 1.00 43.04
	ATOM	1305 CB ARG 329	56.398 27.997 30.482 1.00 43.87
50	ATOM	1306 CG ARG 329	57.258 28.740 29.504 1.00 40.87

	ATOM	1307 CD ARG 329	57.545 27.886 28.314 1.00 39.52
	ATOM	1308 NE ARG 329	58.301 28.643 27.341 1.00 38.90
	ATOM	1309 CZ ARG 329	59.624 28.708 27.313 1.00 40.59
	ATOM	1310 NH1 ARG 329	60.359 28.052 28.196 1.00 42.41
5	ATOM	1311 NH2 ARG 329	60.210 29.466 26.413 1.00 41.87
	ATOM	1312 C ARG 329	56.152 26.817 32.609 1.00 43.00
	ATOM	1313 O ARG 329	55.600 25.716 32.628 1.00 43.66
	ATOM	1314 N SER 330	55.886 27.797 33.456 1.00 41.58
	ATOM	1315 CA SER 330	54.953 27.641 34.538 1.00 40.11
10	ATOM	1316 CB SER 330	55.491 28.362 35.777 1.00 40.38
	ATOM	1317 C SER 330	53.602 28.223 34.103 1.00 38.99
	ATOM	1318 O SER 330	53.553 29.172 33.320 1.00 39.22
	ATOM	1319 N GLY 331	52.517 27.581 34.529 1.00 37.52
	ATOM	1320 CA GLY 331	51.176 28.063 34.232 1.00 35.64
15	ATOM	1321 C GLY 331	50.493 27.782 32.906 1.00 35.14
	ATOM	1322 O GLY 331	49.439 28.363 32.640 1.00 34.48
	ATOM	1323 N LEU 332	51.059 26.925 32.066 1.00 34.54
	ATOM	1324 CA LEU 332	50.424 26.637 30.780 1.00 34.59
	ATOM	1325 CB LEU 332	51.394 25.942 29.828 1.00 33.09
20	ATOM	1326 CG LEU 332	52.532 26.765 29.236 1.00 32.72
	ATOM	1327 CD1 LEU 332	53.473 25.834 28.497 1.00 30.29
	ATOM	1328 CD2 LEU 332	51.987 27.844 28.313 1.00 29.20
	ATOM	1329 C LEU 332	49.191 25.763 30.969 1.00 35.14
	ATOM	1330 O LEU 332	49.178 24.874 31.811 1.00 35.96
25	ATOM	1331 N LEU 333	48.153 26.076 30.204 1.00 35.65
	ATOM	1332 CA LEU 333	46.898 25.345 30.215 1.00 37.97
	ATOM	1333 CB LEU 333	45.743 26.271 29.796 1.00 40.71
	ATOM	1334 CG LEU 333	45.389 27.483 30.670 1.00 43.46
	ATOM ⁻	1335 CD1 LEU 333	44.713 28.620 29.882 1.00 42.72
30	ATOM	1336 CD2 LEU 333	44.487 27.021 31.806 1.00 45.25
	ATOM	1337 C LEU 333	46.952 24.115 29.300 1.00 37.78
	ATOM	1338 O LEU 333	46.695 22.991 29.720 1.00 37.65
	ATOM	1339 N CYA 334	47.361 24.323 28.060 1.00 38.65
	ATOM	1340 CA CYA 334	47.413 23.249 27.073 1.00 40.91
35	ATOM	1341 CB CYA 334	46.936 23.788 25.721 1.00 47.35
	ATOM	1342 SG CYA 334	45.406 24.693 25.867 1.00 52.24
		1343 AS CYA 334	44.066 22.890 25.562 1.00 70.72
		1344 C CYA 334	
	ATOM		
40		1346 N VAL 335	49.329 22.078 27.997 1.00 37.67
		1347 CA VAL 335	50.641 21.432 27.967 1.00 36.07
		1348 CB VAL 335	51.019 20.905 29.384 1.00 33.70
		1349 CG1 VAL 335	52.434 20.332 29.401 1.00 33.70
		1350 CG2 VAL 335	50.913 22.028 30.387 1.00 31.84
45		1351 C VAL 335	50.734 20.334 26.885 1.00 36.09
		1352 O VAL 335	51.662 20.335 26.064 1.00 34.41
		1353 N ASP 336	49.747 19.444 26.833 1.00 35.95
		1354 CA ASP 336	49.748 18.372 25.844 1.00 36.34
		1355 CB ASP 336	48.591 17.394 26.091 1.00 41.36
50	ATOM	1356 CG ASP 336	48.613 16.206 25.129 1.00 46.23

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47.615 16.021 24.392 1.00 49.55
    ATOM 1357 OD1 ASP 336
    ATOM 1358 OD2 ASP 336
                                49.639 15.470 25.097 1.00 48.07
                              49.727 18.846 24.390 1.00 33.05
    ATOM 1359 C ASP 336
                              50.527 18.377 23.573 1.00 32.33
    ATOM 1360 O ASP 336
                              48.794 19.743 24.076 1.00 29.57
    ATOM 1361 N LYS 337
    ATOM 1362 CA LYS 337
                               48.661 20.286 22.723 1.00 27.76
                               47.520 21.313 22.689 1.00 27.09
    ATOM 1363 CB LYS 337
                              49.988 20.941 22.286 1.00 27.64
    ATOM 1364 C LYS 337
    ATOM 1365 O LYS 337
                              50.472 20.713 21.173 1.00 26.09
                              50.597 21.688 23.208 1.00 25.90
    ATOM 1366 N ILE 338
10
                               51.852 22.394 22.971 1.00 24.21
    ATOM 1367 CA ILE 338
                               52.128 23.391 24.122 1.00 23.30
    ATOM 1368 CB ILE 338
                               53.500 24.048 23.958 1.00 21.75
    ATOM 1369 CG2 ILE 338
                               51.014 24.448 24.155 1.00 21.19
    ATOM 1370 CG1 ILE 338
                               51.055 25.393 25.361 1.00 21.39
    ATOM 1371 CD1 ILE 338
15
    ATOM 1372 C ILE 338
                              53.041 21.451 22.782 1.00 25.55
    ATOM 1373 O ILE 338
                              53.861 21.640 21.875 1.00 24.74
    ATOM 1374 N GLU 339
                               53.124 20.421 23.622 1.00 27.43
    ATOM 1375 CA GLU 339
                                54.220 19.448 23.536 1.00 27.60
                                54.201 18.512 24.755 1.00 27.21
    ATOM 1376 CB GLU 339
20
                               54.112 18.650 22.236 1.00 26.85
    ATOM 1377 C GLU 339
                               55.119 18.385 21.581 1.00 26.71
    ATOM 1378 O GLU 339
    ATOM 1379 N LYS 340
                               52.888 18.276 21.872 1.00 27.04
                               52.663 17.515 20.654 1.00 28.19
    ATOM 1380 CA LYS 340
                               51.210 17.008 20.609 1.00 28.67
    ATOM 1381 CB LYS 340
25
    ATOM 1382 C LYS 340
                               53.002 18.402 19.439 1.00 27.96
    ATOM 1383 O LYS 340
                               53.558 17.934 18.436 1.00 27.48
                               52.746 19.700 19.567 1.00 28.32
    ATOM 1384 N SER 341
                               53.058 20.662 18.514 1.00 28.02
    ATOM 1385 CA SER 341
                               52.457 22.022 18.867 1.00 31.25
    ATOM 1386 CB SER 341
30
    ATOM 1387 OG SER 341
                               52.880 23.029 17.965 1.00 37.69
                               54.578 20.773 18.350 1.00 26.01
    ATOM 1388 C SER 341
                               55.096 20.717 17.234 1.00 25.06
    ATOM 1389 O SER 341
                               55.297 20.899 19.462 1.00 25.71
    ATOM 1390 N GLN 342
                                56.750 20.993 19.398 1.00 26.39
    ATOM 1391 CA GLN 342
35
                                57.356 21.254 20.777 1.00 24.17
    ATOM 1392 CB GLN 342
                                58.834 21.590 20.703 1.00 25.09
     ATOM 1393 CG GLN 342
                                59.476 21.677 22.057 1.00 26.93
    ATOM 1394 CD GLN 342
                                59.479 20.704 22.810 1.00 27.77
     ATOM 1395 OE1 GLN 342
    ATOM 1396 NE2 GLN 342
                                60.022 22.839 22.386 1.00 24.61
40
                               57.354 19.715 18.806 1.00 25.69
     ATOM 1397 C GLN 342
                               58.356 19.771 18.075 1.00 24.99
     ATOM 1398 O GLN 342
     ATOM 1399 N GLU 343
                               56.753 18.569 19.127 1.00 25.00
                                57.222 17.280 18.610 1.00 25.34
     ATOM 1400 CA GLU 343
                                56.411 16.118 19.245 1.00 25.90
     ATOM 1401 CB GLU 343
45
                               57.089 17.276 17.076 1.00 24.32
     ATOM 1402 C GLU 343
     ATOM 1403 O GLU 343
                               58.021 16.891 16.365 1.00 23.99
     ATOM 1404 N ALA 344
                               55.961 17.789 16.587 1.00 23.56
                               55.701 17.875 15.153 1.00 22.85
     ATOM 1405 CA ALA 344
                               54.320 18.451 14.917 1.00 22.64
     ATOM 1406 CB ALA 344
50
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	ATOM ATOM	1407 C ALA 344 1408 O ALA 344	56.768 18.743 14.489 1.00 22.77 57.355 18.360 13.477 1.00 22.08
	ATOM	1409 N TYR 345	57.057 19.893 15.092 1.00 21.89
	ATOM	1410 CA TYR 345	58.075 20.792 14.550 1.00 21.18
5	ATOM	1411 CB TYR 345	58.108 22.119 15.313 1.00 20.27
	ATOM	1412 CG TYR 345	57.048 23.078 14.856 1.00 17.45
	ATOM	1413 CD1 TYR 345	56.001 23.431 15.698 1.00 17.99
	ATOM	1414 CE1 TYR 345	54.992 24.253 15.270 1.00 19.97
	ATOM	1415 CD2 TYR 345	57.063 23.589 13.562 1.00 19.11
10	ATOM	1416 CE2 TYR 345	56.055 24.424 13.116 1.00 19.14
	ATOM	1417 CZ TYR 345	55.017 24.749 13.972 1.00 20.78
	ATOM	1418 OH TYR 345	53.983 25.539 13.530 1.00 20.70
	ATOM	1419 C TYR 345	59.454 20.167 14.583 1.00 20.96
	ATOM	1420 O TYR 345	60.221 20.314 13.632 1.00 22.29
15	ATOM	1421 N LEU 346	59.778 19.480 15.677 1.00 20.82
	ATOM	1422 CA LEU 346	61.079 18.838 15.817 1.00 20.18
	ATOM	1423 CB LEU 346	61.216 18.203 17.205 1.00 21.04
	ATOM	1424 CG LEU 346	61.606 19.158 18.335 1.00 21.25
	ATOM	1425 CD1 LEU 346	61.226 18.595 19.685 1.00 20.95
20	ATOM	1426 CD2 LEU 346	63.099 19.438 18.267 1.00 19.90
	ATOM	1427 C LEU 346	61.317 17.806 14.716 1.00 20.19
	ATOM	1428 O LEU 346	62.407 17.755 14.142 1.00 20.69
	ATOM	1429 N LEU 347	60.290 17.016 14.390 1.00 22.00
	ATOM	1430 CA LEU 347	60.406 15.994 13.344 1.00 21.81
25	ATOM	1431 CB LEU 347	59.199 15.051 13.366 1.00 24.03
	ATOM	1432 CG LEU 347	59.301 13.805 14.250 1.00 26.28
	ATOM	1433 CD1 LEU 347	57.964 13.072 14.277 1.00 27.79
	ATOM	1434 CD2 LEU 347	60.409 12.889 13.728 1.00 24.78 60.544 16.623 11.966 1.00 20.50
20	ATOM	1435 C LEU 347	61.351 16.179 11.143 1.00 21.39
30	ATOM	1436 O LEU 347 1437 N ALA 348	59.767 17.674 11.727 1.00 20.84
	ATOM ATOM	1437 N ALA 348 1438 CA ALA 348	59.788 18.381 10.456 1.00 18.12
	ATOM	1439 CB ALA 348	58.729 19.480 10.457 1.00 18.49
	ATOM	1440 C ALA 348	61.168 18.963 10.269 1.00 17.53
35	ATOM	1441 O ALA 348	61.785 18.781 9.228 1.00 18.78
55	ATOM	1442 N PHE 349	61.677 19.569 11.338 1.00 19.55
	ATOM	1443 CA PHE 349	63.001 20.196 11.389 1.00 19.84
		1444 CB PHE 349	63.188 20.823 12.786 1.00 18.68
	ATOM	1445 CG PHE 349	64.380 21.758 12.917 1.00 19.12
40	ATOM	1446 CD1 PHE 349	65.234 22.008 11.851 1.00 19.95
	ATOM	1447 CD2 PHE 349	64.618 22.420 14.126 1.00 20.06
	ATOM	1448 CE1 PHE 349	66.294 22.905 11.971 1.00 18.99
	ATOM	1449 CE2 PHE 349	65.674 23.317 14.261 1.00 16.79
	ATOM	1450 CZ PHE 349	66.516 23.562 13.184 1.00 18.91
45	ATOM	1451 C PHE 349	64.108 19.170 11.103 1.00 20.44
	ATOM	1452 O PHE 349	64.980 19.401 10.260 1.00 19.83
	ATOM	1453 N GLU 350	64.064 18.032 11.794 1.00 23.59
	ATOM	1454 CA GLU 350	65.077 16.995 11.610 1.00 23.46
	ATOM	1455 CB GLU 350	64.830 15.845 12.584 1.00 25.26
50	ATOM	1456 CG GLU 350	65.694 14.644 12.288 1.00 31.98

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ATOM 1457 CD GLU 350
                                65.526 13.482 13.257 1.00 35.49
                                66.560 12.853 13.555 1.00 40.26
     ATOM 1458 OE1 GLU 350
     ATOM 1459 OE2 GLU 350
                                64.380 13.173 13.689 1.00 36.23
                               65.083 16.489 10.165 1.00 21.12
     ATOM 1460 C GLU 350
                               66.133 16.384 9.526 1.00 19.81
     ATOM 1461 O GLU 350
                              63.888 16.234 9.651 1.00 21.98
     ATOM 1462 N HIS 351
                               63.694 15.751 8.292 1.00 21.31
     ATOM 1463 CA HIS 351
    ATOM 1464 CB HIS 351
                               62.238 15.321 8.107 1.00 21.76
     ATOM 1465 CG HIS 351
                               61.839 14.160 8.967 1.00 22.08
     ATOM 1466 CD2 HIS 351
                               62.578 13.317 9.728 1.00 22.65
10
                                60.532 13.751 9.115 1.00 22.37
     ATOM 1467 ND1 HIS 351
                               60.478 12.716 9.930 1.00 21.44
     ATOM 1468 CE1 HIS 351
     ATOM 1469 NE2 HIS 351
                               61.705 12.429 10.314 1.00 20.85
     ATOM 1470 C HIS 351
                              64.117 16.815 7.275 1.00 21.18
                              64.683 16.489 6.231 1.00 22.65
     ATOM 1471 O HIS 351
15
     ATOM 1472 N TYR 352
                               63.915 18.088 7.602 1.00 19.79
                                64.327 19.146 6.697 1.00 18.72
     ATOM 1473 CA TYR 352
     ATOM 1474 CB TYR 352
                                63.768 20.502 7.122 1.00 19.55
     ATOM 1475 CG TYR 352
                                64.140 21.580 6.137 1.00 19.27
                                63.556 21.623 4.867 1.00 19.29
     ATOM 1476 CD1 TYR 352
20
                                63.961 22.555 3.927 1.00 17.55
     ATOM 1477 CE1 TYR 352
                                65.132 22.507 6.438 1.00 18.91
     ATOM 1478 CD2 TYR 352
     ATOM 1479 CE2 TYR 352
                                65.545 23.443 5.503 1.00 17.30
     ATOM 1480 CZ TYR 352
                                64.954 23.459 4.256 1.00 18.41
                                65.355 24.384 3.334 1.00 19.40
    ATOM 1481 OH TYR 352
25
                               65.849 19.182 6.687 1.00 19.31
     ATOM 1482 C TYR 352
     ATOM 1483 O TYR 352
                               66.479 19.333 5.639 1.00 20.25
     ATOM 1484 N VAL 353
                               66,446 19.017 7.858 1.00 21.25
                                67.899 18.993 7.960 1.00 22.03
     ATOM 1485 CA VAL 353
    ATOM 1486 CB VAL 353
                                68.348 18.880 9.450 1.00 22.60
30
                                 69.843 18.635 9.550 1.00 20.34
     ATOM 1487 CG1 VAL 353
    ATOM 1488 CG2 VAL 353
                                 67.997 20.167 10.183 1.00 22.61
                               68.442 17.827 7.108 1.00 22.74
    ATOM 1489 C VAL 353
     ATOM 1490 O VAL 353
                               69.448 17.985 6.398 1.00 23.44
                               67.773 16.674 7.165 1.00 22.30
    ATOM 1491 N ASN 354
35
                                68.185 15.508 6.373 1.00 23.56
    ATOM 1492 CA ASN 354
    ATOM 1493 CB ASN 354
                                67.241 14.320 6.603 1.00 22.26
                                67.374 13.715 7.981 1.00 23.06
     ATOM 1494 CG ASN 354
                                 68.406 13.843 '8.628 1.00 25.79
     ATOM 1495 OD1 ASN 354
                                 66.327 13.044 8.435 1.00 21.07
40
     ATOM 1496 ND2 ASN 354
     ATOM 1497 C ASN 354
                               68.134 15.877 4.888 1.00 25.10
                               69.024 15.534 4.111 1.00 26.70
     ATOM 1498 O ASN 354
     ATOM 1499 N HIS 355
                              67.067 16.568 4.503 1.00 24.50
                               66.881 16.986 3.123 1.00 24.46
     ATOM 1500 CA HIS 355
45
     ATOM 1501 CB HIS 355
                               65.557 17.750 2.969 1.00 26.07
                               65.365 18.337 1.604 1.00 28.28
     ATOM 1502 CG HIS 355
                                65.918 19.422 1.018 1.00 28.10
     ATOM 1503 CD2 HIS 355
     ATOM 1504 ND1 HIS 355
                                64.600 17.724 0.632 1.00 26.32
     ATOM 1505 CE1 HIS 355
                               64.706 18.407 -0.499 1.00 27.71
                               65.502 19.435 -0.288 1.00 27.79
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     ATOM 1506 NE2 HIS 355
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ATOM 1507 C HIS 355
                              68.022 17.857 2.624 1.00 24.07
                              68.460 17.729 1.484 1.00 23.54
    ATOM 1508 O HIS 355
    ATOM 1509 N ARG 356
                               68.463 18.774 3.471 1.00 25.31
    ATOM 1510 CA ARG 356
                                69.523 19.714 3.130 1.00 25.69
                                69.561 20.820 4.168 1.00 24.06
    ATOM 1511 CB ARG 356
                                68.337 21.682 4.094 1.00 23.23
    ATOM 1512 CG ARG 356
                                68.670 22.973 3.424 1.00 25.91
    ATOM 1513 CD ARG 356
    ATOM 1514 NE ARG 356
                                69.447 23.814 4.322 1.00 24.87
                                70.325 24.726 3.928 1.00 25.05
    ATOM 1515 CZ ARG 356
    ATOM 1516 NH1 ARG 356
                                70.546 24.920 2.640 1.00 24.97
10
                                70.978 25.453 4.831 1.00 25.62
    ATOM 1517 NH2 ARG 356
                               70.900 19.109 2.949 1.00 27.73
    ATOM 1518 C ARG 356
    ATOM 1519 O ARG 356
                               71.724 19.645 2.208 1.00 28.38
                               71.179 18.048 3.693 1.00 29.45
    ATOM 1520 N LYS 357
                               72.457 17.355 3.588 1.00 31.35
    ATOM 1521 CA LYS 357
15
                               72.503 16.566 2.270 1.00 32.80
    ATOM 1522 CB LYS 357
    ATOM 1523 CG LYS 357
                               71.290 15.650 2.103 1.00 35.78
                               71.264 14.927 0.778 1.00 39.43
    ATOM 1524 CD LYS 357
    ATOM 1525 CE LYS 357
                               70.121 13.918 0.739 1.00 42.93
                               70.162 13.074 -0.498 1.00 45.97
20
    ATOM 1526 NZ LYS 357
                               73.692 18.247 3.743 1.00 31.34
    ATOM 1527 C LYS 357
    ATOM 1528 O LYS 357
                               74.489 18.390 2.818 1.00 32.65
                              73.837 18.861 4.913 1.00 30.72
    ATOM 1529 N HIS 358
    ATOM 1530 CA HIS 358
                               74.995 19.706 5.186 1.00 31.49
                               74.895 20.322 6.579 1.00 29.13
25
    ATOM 1531 CB HIS 358
                               73.882 21.415 6.688 1.00 25.30
    ATOM 1532 CG HIS 358
                               74.026 22.760 6.646 1.00 24.90
    ATOM 1533 CD2 HIS 358
    ATOM 1534 ND1 HIS 358
                               72.543 21.175 6.892 1.00 24.54
                               71.901 22.324 6.975 1.00 23.68
     ATOM 1535 CE1 HIS 358
                               72.777 23.302 6.830 1.00 25.28
    ATOM 1536 NE2 HIS 358
30
                              76.235 18.831 5.161 1.00 33.38
     ATOM 1537 C HIS 358
                              76.166 17.647 5.495 1.00 35.46
    ATOM 1538 O HIS 358
                               77.366 19.399 4.768 1.00 35.34
    ATOM 1539 N ASN 359
                                78.606 18.636 4.746 1.00 38.17
    ATOM 1540 CA ASN 359
                               79.544 19.150 3.646 1.00 37.84
    ATOM 1541 CB ASN 359
35
                               79.236 18.825 6.120 1.00 39.85
     ATOM 1542 C ASN 359
    ATOM 1543 O ASN 359
                               80.317 19.406 6.240 1.00 42.72
                              78.510 18.411 7.159 1.00 39.01
     ATOM 1544 N ILE 360
                               78.968 18.526 8.549 1.00 36.72
     ATOM 1545 CA ILE 360
                               78.351 19.752 9.264 1.00 37.69
     ATOM 1546 CB ILE 360
40
     ATOM 1547 CG2 ILE 360
                               78.802 19.793 10.722 1.00 37.56
                               78,735 21,049 8,549 1,00 37,68
     ATOM 1548 CG1 ILE 360
                               77.970 22.253 9.041 1.00 38.40
     ATOM 1549 CD1 ILE 360
                              78.524 17.278 9.303 1.00 35.15
     ATOM 1550 C ILE 360
                              77.343 16.931 9.314 1.00 33.75
45
     ATOM 1551 O ILE 360
                               79.475 16.564 9.912 1.00 34.64
     ATOM 1552 N PRO 361
                               80.930 16.785 9.873 1.00 35.59
     ATOM 1553 CD PRO 361
                                79.138 15.349 10.660 1.00 33.92
     ATOM 1554 CA PRO 361
                                80.513 14.768 11.014 1.00 35.27
     ATOM 1555 CB PRO 361
                                81.412 15.972 11.048 1.00 35.97
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    ATOM 1556 CG PRO 361
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ATOM 1557 C PRO 361
                               78.292 15.618 11.909 1.00 30.95
     ATOM 1558 O PRO 361
                               78.555 16.554 12.653 1.00 31.50
     ATOM 1559 N HIS 362
                               77.269 14.793 12.112 1.00 28.75
                               76.378 14.900 13.263 1.00 30.25
     ATOM 1560 CA HIS 362
     ATOM 1561 CB HIS 362
                               77.152 14.612 14.548 1.00 31.20
     ATOM 1562 CG HIS 362
                               78.075 13.441 14.440 1.00 33.72
                                77.826 12.122 14.275 1.00 34.55
     ATOM 1563 CD2 HIS 362
     ATOM 1564 ND1 HIS 362
                                79.449 13.569 14.469 1.00 35.55
                                80.006 12.377 14.322 1.00 35.28
     ATOM 1565 CE1 HIS 362
                                79.040 11.484 14.204 1.00 37.61
10
     ATOM 1566 NE2 HIS 362
     ATOM 1567 C HIS 362
                               75.742 16.275 13.368 1.00 29.44
     ATOM 1568 O HIS 362
                               75.521 16.769 14.472 1.00 29.93
                               75.397 16.856 12.222 1.00 29.22
     ATOM 1569 N PHE 363
     ATOM 1570 CA PHE 363
                                74.803 18.188 12.160 1.00 27.72
     ATOM 1571 CB PHE 363
                                74.446 18.538 10.709 1.00 26.85
15
     ATOM 1572 CG PHE 363
                                73.901 19.931 10.532 1.00 27.48
                                74.758 21.017 10.391 1.00 27.76
     ATOM 1573 CD1 PHE 363
     ATOM 1574 CD2 PHE 363
                                72.523 20.157 10.513 1.00 27.45
    ATOM 1575 CE1 PHE 363
                                74.244 22.313 10.234 1.00 28.56
                                72.001 21.446 10.357 1.00 25.15
20
     ATOM 1576 CE2 PHE 363
    ATOM 1577 CZ PHE 363
                                72.860 22.521 10.219 1.00 24.41
     ATOM 1578 C PHE 363
                               73.597 18.385 13.075 1.00 27.45
    ATOM 1579 O PHE 363
                               73.577 19.324 13.880 1.00 27.73
                               72.616 17.489 12.983 1.00 25.89
     ATOM 1580 N TRP 364
25
     ATOM 1581 CA TRP 364
                               71.401 17.592 13.800 1.00 25.85
    ATOM 1582 CB TRP 364
                                70.444 16.426 13.506 1.00 24.27
                                69.168 16.391 14.328 1.00 23.75
    ATOM 1583 CG TRP 364
                                68.152 17.407 14.397 1.00 24.87
    ATOM 1584 CD2 TRP 364
                                67.140 16.922 15.261 1.00 24.81
     ATOM 1585 CE2 TRP 364
30
    ATOM 1586 CE3 TRP 364
                                67.989 18.674 13.820 1.00 25.47
                                68.745 15.370 15.122 1.00 22.98
     ATOM 1587 CD1 TRP 364
     ATOM 1588 NE1 TRP 364
                                67.530 15.679 15.684 1.00 25.99
     ATOM 1589 CZ2 TRP 364
                                65.987 17.661 15.560 1.00 25.14
     ATOM 1590 CZ3 TRP 364
                                66.844 19.405 14.116 1.00 25.29
    ATOM 1591 CH2 TRP 364
                                65.857 18.894 14.982 1.00 24.53
35
                               71.659 17.747 15.308 1.00 26.94
     ATOM 1592 C TRP 364
                               71.202 18.721 15.904 1.00 27.16
    ATOM 1593 O TRP 364
    ATOM 1594 N PRO 365
                               72.382 16.796 15.944 1.00 27.60
                                72.912 15.522 15.411 1.00 27.55
     ATOM 1595 CD PRO 365
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    ATOM 1596 CA PRO 365
                                72.655 16.915 17.387 1.00 25.90
     ATOM 1597 CB PRO 365
                                73.565 15.717 17.668 1.00 26.00
     ATOM 1598 CG PRO 365
                                73.136 14.705 16.658 1.00 28.32
     ATOM 1599 C PRO 365
                               73.374 18.225 17.714 1.00 23.89
     ATOM 1600 O PRO 365
                               73.088 18.861 18.725 1.00 23.81
    ATOM 1601 N LYS 366
                               74.297 18.626 16.845 1.00 24.24
45
                                75.058 19.862 17.027 1.00 26.24
     ATOM 1602 CA LYS 366
     ATOM 1603 CB LYS 366
                                76.144 19.982 15.963 1.00 27.44
     ATOM 1604 CG LYS 366
                                77.310 19.022 16.138 1.00 28.76
                                78.254 19.171 14.975 1.00 30.53
     ATOM 1605 CD LYS 366
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    ATOM 1606 CE LYS 366
                                79.527 18.387 15.167 1.00 34.25
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	ATOM	1607 NZ LYS 366	80.388 18.463 13.947 1.00 37.89
	ATOM	1608 C LYS 366	74.181 21.107 16.993 1.00 26.73
	ATOM	1609 O LYS 366	74.385 22.042 17.762 1.00 27.36
	ATOM	1610 N LEU 367	73.216 21.124 16.086 1.00 27.98
5	ATOM	1611 CA LEU 367	72.308 22.256 15.967 1.00 27.87
	ATOM	1612 CB LEU 367	71.559 22.192 14.632 1.00 27.29
	ATOM	1613 CG LEU 367	70.613 23.356 14.318 1.00 27.25
	ATOM	1614 CD1 LEU 367	71.334 24.707 14.510 1.00 22.90
	ATOM	1615 CD2 LEU 367	70.081 23.189 12.896 1.00 24.54
10	ATOM	1616 C LEU 367	71.327 22.223 17.134 1.00 29.38
	ATOM	1617 O LEU 367	70.993 23.249 17.716 1.00 31.09
	ATOM	1618 N LEU 368	70.889 21.026 17.491 1.00 30.38
	ATOM	1619 CA LEU 368	69.962 20.843 18.594 1.00 31.14
	ATOM	1620 CB LEU 368	69.659 19.353 18.731 1.00 32.20
15	ATOM	1621 CG LEU 368	68.247 18.852 19.014 1.00 33.52
	ATOM	1622 CD1 LEU 368	67.184 19.651 18.267 1.00 31.14
	ATOM	1623 CD2 LEU 368	68.210 17.379 18.632 1.00 33.99
	ATOM	1624 C LEU 368	70.601 21.395 19.876 1.00 32.36
	ATOM	1625 O LEU 368	69.917 21.963 20.730 1.00 32.58
20	ATOM	1626 N MET 369	71.922 21.272 19.985 1.00 33.30
	ATOM	1627 CA MET 369	72.641 21.771 21.149 1.00 34.04
	ATOM	1628 CB MET 369	74.051 21.190 21.209 1.00 35.31
	ATOM	1629 CG MET 369	74.108 19.858 21.935 1.00 36.83
	ATOM	1630 SD MET 369	75.312 18.728 21.235 1.00 43.07
25	ATOM	1631 CE MET 369	76.862 19.636 21.472 1.00 41.31
	ATOM	1632 C MET 369	72.675 23.297 21.212 1.00 34.30
	ATOM	1633 O MET 369	72.961 23.876 22.269 1.00 35.82
	ATOM	1634 N LYS 370	72.368 23.949 20.091 1.00 32.14
	ATOM	1635 CA LYS 370	72.325 25.405 20.044 1.00 29.17
30	ATOM	1636 CB LYS 370	72.394 25.904 18.608 1.00 28.18
	ATOM	1637 CG LYS 370	73.662 25.518 17.900 1.00 27.72
	ATOM	1638 CD LYS 370	74.866 25.969 18.679 1.00 28.10
	ATOM	1639 CE LYS 370	76.127 25.650 17.930 1.00 27.79
	ATOM	1640 NZ LYS 370	77.298 25.941 18.777 1.00 30.78
35	ATOM	1641 C LYS 370	71.033 25.875 20.705 1.00 29.27
	ATOM	1642 O LYS 370	70.950 26.999 21.200 1.00 29.43
	ATOM	1643 N VAL 371	70.018 25.014 20.714 1.00 29.40
	ATOM	1644 CA VAL 371	68.756 25.358 21.358 1.00 29.90
	ATOM	1645 CB VAL 371	67.687 24.237 21.218 1.00 28.75
40	ATOM	1646 CG1 VAL 371	66.463 24.561 22.064 1.00 27.12
	ATOM	1647 CG2 VAL 371	67.275 24.080 19.762 1.00 29.23
	ATOM	1648 C VAL 371	69.075 25.573 22.832 1.00 31.39
	ATOM	1649 O VAL 371	68.543 26.481 23.462 1.00 31.20
	ATOM	1650 N THR 372	69.971 24.743 23.366 1.00 31.39
45	ATOM	1651 CA THR 372	70.371 24.847 24.762 1.00 31.10
	ATOM	1652 CB THR 372	71.282 23.664 25.170 1.00 31.59
	ATOM	1653 OG1 THR 372	70.554 22.441 25.008 1.00 30.60
	ATOM	1654 CG2 THR 372	71.720 23.795 26.625 1.00 30.14
	ATOM	1655 C THR 372	71.071 26.186 24.994 1.00 30.76
50	ATOM	1656 O THR 372	70.711 26.935 25.910 1.00 31.45

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72.038 26.507 24.138 1.00 29.31
    ATOM 1657 N ASP 373
    ATOM 1658 CA ASP 373
                               72.744 27.772 24.252 1.00 27.32
                               73.745 27.934 23.115 1.00 27.98
    ATOM 1659 CB ASP 373
                               74.886 26.933 23.190 1.00 28.94
    ATOM 1660 CG ASP 373
                                75.043 26.259 24.225 1.00 31.01
    ATOM 1661 OD1 ASP 373
                                75.639 26.825 22.205 1.00 31.38
    ATOM 1662 OD2 ASP 373
                              71.742 28.926 24.247 1.00 26.50
    ATOM 1663 C ASP 373
                              71.872 29.861 25.040 1.00 27.35
    ATOM 1664 O ASP 373
    ATOM 1665 N LEU 374
                               70.711 28.826 23.412 1.00 24.17
                               69.688 29.864 23.331 1.00 23.38
    ATOM 1666 CA LEU 374
10
                               68.795 29.660 22.107 1.00 22.98
    ATOM 1667 CB LEU 374
                                69.361 30.183 20.786 1.00 24.45
    ATOM 1668 CG LEU 374
                                68.668 29.520 19.589 1.00 24.72
    ATOM 1669 CD1 LEU 374
                                69.223 31.704 20.735 1.00 22.40
    ATOM 1670 CD2 LEU 374
                               68.839 29.964 24.589 1.00 24.31
    ATOM 1671 C LEU 374
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                               68.442 31.065 24.986 1.00 23.31
    ATOM 1672 O LEU 374
    ATOM 1673 N ARG 375
                               68.543 28.826 25.211 1.00 25.32
    ATOM 1674 CA ARG 375
                                67.748 28.821 26.438 1.00 27.76
                                67.455 27.392 26.908 1.00 30.82
    ATOM 1675 CB ARG 375
                                66.901 26.439 25.854 1.00 38.79
    ATOM 1676 CG ARG 375
20
                                65,424 26.630 25.582 1.00 45.40
    ATOM 1677 CD ARG 375
                                64.709 25.360 25.620 1.00 52.61
    ATOM 1678 NE ARG 375
    ATOM 1679 CZ ARG 375
                                63.800 24.967 24.726 1.00 56.89
                                 63.473 25.732 23.694 1.00 58.27
    ATOM 1680 NH1 ARG 375
                                 63.201 23.793 24.855 1.00 58.46
    ATOM 1681 NH2 ARG 375
25
                               68.563 29.542 27.512 1.00 26.98
    ATOM 1682 C ARG 375
    ATOM 1683 O ARG 375
                               68.025 30.336 28.282 1.00 26.18
                               69.862 29.255 27.551 1.00 26.80
    ATOM 1684 N MET 376
                                70.767 29.867 28.511 1.00 29.22
    ATOM 1685 CA MET 376
                                72.172 29.270 28.379 1.00 33.70
    ATOM 1686 CB MET 376
30
                                72.595 28.371 29.562 1.00 43.20
    ATOM 1687 CG MET 376
                             73.320 29.260 31.011 1.00 52.38
    ATOM 1688 SD MET 376
                                71.843 29.854 31.913 1.00 48.11
    ATOM 1689 CE MET 376
                               70,804 31.384 28.339 1.00 27.54
    ATOM 1690 C MET 376
                               70.792 32.126 29.323 1.00 26.96
    ATOM 1691 O MET 376
35
                              70.841 31.835 27.087 1.00 25.39
    ATOM 1692 N ILE 377
                               70.847 33.264 26.767 1.00 23.26
    ATOM 1693 CA ILE 377
                               70.992 33.488 25.222 1.00 22.73
    ATOM 1694 CB ILE 377
                               70.560 34.909 24.819 1.00 21.81
    ATOM 1695 CG2 ILE 377
    ATOM 1696 CG1 ILE 377
                               72.431 33.205 24.789 1.00 20.39
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    ATOM 1697 CD1 ILE 377
                                72.644 33.148 23.300 1.00 18.85
                              69.558 33.900 27.309 1.00 22.91
    ATOM 1698 C ILE 377
                              69.597 34.925 27.989 1.00 22.02
     ATOM 1699 O ILE 377
                               68.427 33.244 27.069 1.00 22.29
    ATOM 1700 N GLY 378
                                67.161 33.757 27.547 1.00 22.83
    ATOM 1701 CA GLY 378
45
                               67.111 33.815 29.063 1.00 25.60
    ATOM 1702 C GLY 378
     ATOM 1703 O GLY 378
                               66.546 34.752 29.630 1.00 26.25
                               67.691 32.804 29.713 1.00 26.88
     ATOM 1704 N ALA 379
                               67.744 32.707 31.175 1.00 27.19
     ATOM 1705 CA ALA 379
                                68.322 31.358 31.590 1.00 26.97
     ATOM 1706 CB ALA 379
50
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	ATOM	1707 C ALA 379 68.606 33.827 31.738 1.00 26.13
	ATOM	1708 O ALA 379 68.174 34.580 32.601 1.00 26.46
	ATOM	1709 N CYA 380 69.826 33.935 31.230 1.00 27.61
_	ATOM	1710 CA CYA 380 70.742 34.973 31.667 1.00 29.74
5	ATOM	1711 CB CYA 380 72.070 34.865 30.923 1.00 35.44
	ATOM	1712 SG CYA 380 73.081 33.458 31.417 1.00 42.61
	ATOM	1713 AS CYA 380 74.829 33.691 29.945 1.00 55.91
	ATOM	1714 C CYA 380 70.142 36.349 31.446 1.00 29.07
	ATOM	1715 O CYA 380 70.243 37.225 32.303 1.00 29.46
10	ATOM	1716 N HIS 381 69.494 36.538 30.304 1.00 28.29
	ATOM	1717 CA HIS 381 68.885 37.824 30.002 1.00 26.84
	ATOM	1718 CB HIS 381 68.384 37.880 28.557 1.00 23.13
	ATOM	1719 CG HIS 381 67.597 39.113 28.259 1.00 19.84
	ATOM	1720 CD2 HIS 381 67.993 40.365 27.931 1.00 18.68
15	ATOM	1721 ND1 HIS 381 66.229 39.169 28.403 1.00 19.47
	ATOM	1722 CE1 HIS 381 65.817 40.407 28.190 1.00 18.64
	ATOM	1723 NE2 HIS 381 66.868 41.149 27.900 1.00 18.29
•	ATOM	1724 C HIS 381 67.747 38.157 30.967 1.00 26.78
	ATOM	1725 O HIS 381 67.560 39.314 31.337 1.00 26.39
20	ATOM	1726 N ALA 382 66.964 37.158 31.347 1.00 27.78
	ATOM	1727 CA ALA 382 65.867 37.395 32.269 1.00 29.45
	ATOM	1728 CB ALA 382 65.077 36.125 32.471 1.00 29.51
	ATOM	1729 C ALA 382 66.425 37.904 33.604 1.00 31.74
	ATOM	1730 O ALA 382 65.932 38.882 34.159 1.00 32.60
25	ATOM	1731 N SER 383 67.483 37.262 34.093 1.00 33.02
	ATOM	1732 CA SER 383 68.109 37.662 35.350 1.00 34.69
	ATOM	1733 CB SER 383 69.212 36.677 35.733 1.00 36.18
	ATOM	1734 OG SER 383 68.663 35.386 35.933 1.00 40.61
	ATOM	1735 C SER 383 68.689 39.064 35.242 1.00 33.49
30	ATOM	1736 O SER 383 68.526 39.889 36.146 1.00 34.28
	ATOM	1737 N ARG 384 69.377 39.332 34.141 1.00 32.60
	ATOM	1738 CA ARG 384 69.955 40.642 33.938 1.00 32.60
	ATOM	1739 CB ARG 384 70.926 40.638 32.762 1.00 33.60
	ATOM	1740 CG ARG 384 71.429 42.013 32.409 1.00 36.33
35	ATOM	1741 CD ARG 384 72.875 41.975 31.993 1.00 39.62
	ATOM	1742 NE ARG 384 73.760 42.260 33.114 1.00 41.76
	ATOM	1743 CZ ARG 384 74.587 43.301 33.179 1.00 41.92
		1744 NH1 ARG 384 74.670 44.182 32.191 1.00 40.66
	ATOM	1745 NH2 ARG 384 75.319 43.471 34.260 1.00 44.88
40	ATOM	1746 C ARG 384 68.862 41.694 33.758 1.00 32.28
	ATOM	1747 O ARG 384 69.014 42.831 34.213 1.00 33.27
	ATOM	1748 N PHE 385 67.739 41.311 33.159 1.00 29.13
	ATOM	1749 CA PHE 385 66.663 42.259 32.977 1.00 27.55
	ATOM	1750 CB PHE 385 65.552 41.687 32.105 1.00 26.89
45	ATOM	1751 CG PHE 385 64.415 42.641 31.888 1.00 25.11
	ATOM	1752 CD1 PHE 385 64.495 43.630 30.918 1.00 24.94
	ATOM	1753 CD2 PHE 385 63.281 42.580 32.689 1.00 25.01
	ATOM	1754 CE1 PHE 385 63.466 44.547 30.753 1.00 25.50
	ATOM	1755 CE2 PHE 385 62.244 43.495 32.531 1.00 24.06
50	ATOM	1756 CZ PHE 385 62.338 44.482 31.563 1.00 25.44

```
66.125 42.641 34.348 1.00 29.08
    ATOM 1757 C PHE 385
                               65.887 43.816 34.613 1.00 27.90
    ATOM 1758 O PHE 385
    ATOM 1759 N LEU 386
                               65.972 41.658 35.231 1.00 31.19
                               65.465 41.929 36.577 1.00 33.22
    ATOM 1760 CA LEU 386
                                65,355 40,640 37,397 1,00 34,35
    ATOM 1761 CB LEU 386
    ATOM 1762 C LEU 386
                               66.362 42.940 37.279 1.00 33.52
                               65.874 43.907 37.855 1.00 32.93
    ATOM 1763 O LEU 386
                              67.673 42.760 37.158 1.00 34.80
    ATOM 1764 N HIS 387
                               68.628 43.674 37.775 1.00 37.88
    ATOM 1765 CA HIS 387
    ATOM 1766 CB HIS 387
                               70.042 43.112 37.705 1.00 36.66
10
                               70.206 41.832 38.456 1.00 39.14
    ATOM 1767 CG HIS 387
                                69.307 41.080 39.144 1.00 39.28
    ATOM 1768 CD2 HIS 387
    ATOM 1769 ND1 HIS 387
                                71.408 41.161 38.543 1.00 40.97
                               71.241 40.055 39.245 1.00 41.57
    ATOM 1770 CE1 HIS 387
                               69.980 39.984 39.618 1.00 41.45
    ATOM 1771 NE2 HIS 387
15
                              68.589 45.071 37.164 1.00 40.38
    ATOM 1772 C HIS 387
                              68.673 46.054 37.888 1.00 40.87
    ATOM 1773 O HIS 387
                               68.466 45.161 35.842 1.00 43.32
    ATOM 1774 N MET 388
                                68.398 46.455 35.168 1.00 46.28
    ATOM 1775 CA MET 388
                                68.170 46.286 33.665 1.00 43.30
    ATOM 1776 CB MET 388
20
                                69.342 45.738 32.875 1.00 43.55
    ATOM 1777 CG MET 388
                                69.034 45.896 31.098 1.00 46.27
    ATOM 1778 SD MET 388
     ATOM 1779 CE MET 388
                                68.208 44.370 30.709 1.00 42.36
     ATOM 1780 C MET 388
                               67.256 47.289 35.737 1.00 50.25
                               67.363 48.506 35.886 1.00 49.79
    ATOM 1781 O MET 388
25
                               66.163 46.610 36.075 1.00 52.74
                                                              ALTA
     ATOM 1782 N LYS 389
                                64.983 47.274 36.633 1.00 56.15
                                                              ALTA
     ATOM 1783 CA LYS 389
     ATOM 1784 CB LYS 389
                                63.770 46.334 36.565 1.00 56.87
                                                              ALTA
                                63.227 46.087 35.161 1.00 57.76
                                                              ALTA
    ATOM 1785 CG LYS 389
                                62.029 45.156 35.212 1.00 55.98
                                                              ALTA
    ATOM 1786 CD LYS 389
30
                                62.426 43.796 35.778 1.00 55.48
                                                              ALTA
     ATOM 1787 CE LYS 389
                               61.267 43.040 36.311 1.00 55.55
                                                              ALTA
    ATOM 1788 NZ LYS 389
                               65.177 47.767 38.064 1.00 56.69
                                                             ALTA
     ATOM 1789 C LYS 389
     ATOM 1790 O LYS 389
                               64.623 48.814 38.453 1.00 58.54
                                                             ALTA
     ATOM 1791 N VAL 390
                               65.955 47.038 38.839 1.00 55.21
35
                                66.225 47.386 40.236 1.00 51.78
     ATOM 1792 CA VAL 390
                                66.999 46.231 40.985 1.00 50.07
     ATOM 1793 CB VAL 390
     ATOM 1794 CG1 VAL 390
                                67.648 46.726 42.263 1.00 49.74
                                 66.037 45.093 41.317 1.00 49.06
     ATOM 1795 CG2 VAL 390
                               67.053 48.681 40.227 1.00 49.38
     ATOM 1796 C VAL 390
                               66.785 49.605 40.992 1.00 48.71
     ATOM 1797 O VAL 390
                               67.974 48.778 39.272 1.00 46.71
     ATOM 1798 N GLU 391
                                68.866 49.919 39.142 1.00 44.88
     ATOM 1799 CA GLU 391
                                70.156 49.488 38.438 1.00 45.24
     ATOM 1800 CB GLU 391
                                70.793 48.207 38.997 1.00 47.65
     ATOM 1801 CG GLU 391
45
                                71.461 48.388 40.358 1.00 50.29
     ATOM 1802 CD GLU 391
                                71.141 49.373 41.063 1.00 50.68
     ATOM 1803 OE1 GLU 391
     ATOM 1804 OE2 GLU 391
                                 72.310 47.535 40.718 1.00 50.85
                               68.324 51.174 38.458 1.00 45.28
     ATOM 1805 C GLU 391
                               68.568 52.286 38.940 1.00 46.46
     ATOM 1806 O GLU 391
50
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	ATOM	1807 N CYA 392	67.568 51.024 37.372 1.00 43.33
	ATOM	1808 CA CYA 392	67.071 52.192 36.643 1.00 42.28
	ATOM	1809 CB CYA 392	67.519 52.096 35.197 1.00 42.45
	ATOM	1810 SG CYA 392	69.280 52.182 35.127 1.00 43.69
5	ATOM	18P1 AS CYA 392	69.908 51.044 33.336 1.00 48.17
_	ATOM	1812 C CYA 392	65.589 52.493 36.709 1.00 42.51
	ATOM	1813 O CYA 392	64.792 51.634 37.070 1.00 43.30
	ATOM	1814 N PRO 393	65.205 53.752 36.418 1.00 42.13
	ATOM	1815 CD PRO 393	66.109 54.899 36.199 1.00 40.54
10	ATOM	1816 CA PRO 393	63.794 54.182 36.441 1.00 42.26
	ATOM	1817 CB PRO 393	63.896 55.710 36.365 1.00 41.47
	ATOM	1818 CG PRO 393	65.189 55.938 35.614 1.00 41.10
	ATOM	1819 C PRO 393	62.954 53.606 35.281 1.00 43.20
	ATOM	1820 O PRO 393	63.463 53.452 34.163 1.00 42.61
15	ATOM	1821 N THR 394	61.686 53.305 35.559 1.00 43.70
	ATOM	1822 CA THR 394	60.764 52.755 34.564 1.00 45.50
	ATOM	1823 CB THR 394	59.340 52.609 35.129 1.00 47.20
	ATOM	1824 OG1 THR 394	59.304 53.139 36.464 1.00 50.57
	ATOM	1825 CG2 THR 394	58.878 51.150 35.137 1.00 47.99
20	ATOM	1826 C THR 394	60.682 53.583 33.283 1.00 44.58
	ATOM	1827 O THR 394	60.409 53.054 32.215 1.00 46.36
	ATOM	1828 N GLU 395	60.899 54.888 33.396 1.00 42.88
	ATOM	1829 CA GLU 395	60.842 55.790 32.246 1.00 40.54
	ATOM	1830 CB GLU 395	61.096 57.234 32.699 1.00 40.69
25	ATOM	1831 C GLU 395	61.799 55.421 31.098 1.00 38.51
	ATOM	1832 O GLU 395	61.628 55.877 29.968 1.00 39.41
	ATOM	1833 N LEU 396	62.828 54.640 31.402 1.00 35.60
	ATOM	1834 CA LEU 396	63.795 54.220 30.386 1.00 33.11
	ATOM	1835 CB LEU 396	65.169 54.003 31.027 1.00 33.60
30	ATOM	1836 CG LEU 396	65.831 55.230 31.660 1.00 34.54
•	ATOM	1837 CD1 LEU 396	67.160 54.835 32.282 1.00 32.83
	ATOM	1838 CD2 LEU 396	66.026 56.308 30.599 1.00 35.71
	ATOM	1839 C LEU 396	63.388 52.940 29.660 1.00 30.95
	ATOM	1840 O LEU 396	63.950 52.605 28.624 1.00 30.90
35	ATOM	1841 N PHE 397	62.422 52.227 30.223 1.00 30.18
	ATOM	1842 CA PHE 397	61.961 50.970 29.654 1.00 28.80
	ATOM	1843 CB PHE 397	61.712 49.946 30.777 1.00 28.10
	ATOM	1844 CG PHE 397	62.938 49.604 31.592 1.00 28.96
40	ATOM	1845 CD1 PHE 397	63.403 50.472 32.591 1.00 28.39
40	ATOM	1846 CD2 PHE 397	63.636 48.422 31.359 1.00 26.28 64.546 50.166 33.337 1.00 28.44
	ATOM	1847 CE1 PHE 397	64.784 48.107 32.103 1.00 29.21
	ATOM	1848 CE2 PHE 397	65.240 48.984 33.096 1.00 27.37
	ATOM	1849 CZ PHE 397	60.683 51.093 28.836 1.00 27.54
45	ATOM	1850 C PHE 397	59.630 51.431 29.370 1.00 26.96
45	ATOM	1851 O PHE 397	
	ATOM	1852 N PRO 398	60.753 50.836 27.501 1.00 27.41 61.968 50.600 26.686 1.00 25.42
	ATOM	1853 CD PRO 398	59,560 50,920 26.654 1.00 25.90
	ATOM	1854 CA PRO 398	60.068 50.383 25.320 1.00 25.26
50	ATOM	1855 CB PRO 398 1856 CG PRO 398	61.490 50.893 25.290 1.00 23.99
50	ATOM	1856 CG PRO 398	01.490 30.693 23.290 1.00 23.99

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58.494 49.995 27.272 1.00 25.86
    ATOM 1857 C PRO 398
    ATOM 1858 O PRO 398
                              58.839 48.962 27.843 1.00 25.82
                              57.197 50.355 27.175 1.00 25.52
    ATOM 1859 N PRO 399
                              56.627 51.576 26.578 1.00 25.49
    ATOM 1860 CD PRO 399
                               56.145 49.510 27.754 1.00 25.42
    ATOM 1861 CA PRO 399
                               54.861 50.181 27.273 1.00 26.23
    ATOM 1862 CB PRO 399
                               55.237 51.609 27.156 1.00 25.25
    ATOM 1863 CG PRO 399
    ATOM 1864 C PRO 399
                               56.198 48.043 27.317 1.00 26.08
    ATOM 1865 O PRO 399
                               56.132 47.131 28.159 1.00 25.45
                              56.350 47.810 26.019 1.00 25.57
    ATOM 1866 N LEU 400
10
                              56.406 46.440 25.509 1.00 26.27
    ATOM 1867 CA LEU 400
                               56.404 46.418 23.980 1.00 25.03
    ATOM 1868 CB LEU 400
                               56.117 45.042 23.363 1.00 24.51
    ATOM 1869 CG LEU 400
    ATOM 1870 CD1 LEU 400
                                54.757 44.530 23.806 1.00 23.22
                                56.173 45.149 21.862 1.00 23.70
    ATOM 1871 CD2 LEU 400
15
                              57.602 45.657 26.067 1.00 27.06
    ATOM 1872 C LEU 400
                              57.484 44.465 26.363 1.00 27.41
    ATOM 1873 O LEU 400
    ATOM 1874 N PHE 401
                              58.736 46.339 26.231 1.00 27.16
                               59.966 45.754 26.779 1.00 27.06
    ATOM 1875 CA PHE 401
                               61.047 46.833 26.802 1.00 26.60
    ATOM 1876 CB PHE 401
20
                               62.408 46.351 27.217 1.00 28.08
    ATOM 1877 CG PHE 401
    ATOM 1878 CD1 PHE 401
                               62.918 45.138 26.747 1.00 27.45
    ATOM 1879 CD2 PHE 401
                                63.223 47.165 28.013 1.00 27.48
                               64.220 44.746 27.055 1.00 26.95
    ATOM 1880 CE1 PHE 401
                               64.523 46.786 28.327 1.00 27.97
    ATOM 1881 CE2 PHE 401
25
                               65.028 45.575 27.846 1.00 28.46
    ATOM 1882 CZ PHE 401
    ATOM 1883 C PHE 401
                              59.690 45.247 28.205 1.00 27.62
                              60.046 44.125 28.570 1.00 26.24
    ATOM 1884 O PHE 401
                               59.036 46.082 29.002 1.00 28.75
    ATOM 1885 N LEU 402
    ATOM 1886 CA LEU 402 58.692 45.719 30.366 1.00 29.58
30
                               58.064 46.910 31.088 1.00 30.04
    ATOM 1887 CB LEU 402
                               59.025 47.974 31.594 1.00 30.14
    ATOM 1888 CG LEU 402
    ATOM 1889 CD1 LEU 402
                                58.270 49.263 31.880 1.00 29.61
                                59.734 47.438 32.827 1.00 27.99
    ATOM 1890 CD2 LEU 402
                              57.693 44.583 30.368 1.00 30.10
    ATOM 1891 C LEU 402
35
    ATOM 1892 O LEU 402
                               57.836 43.631 31.121 1.00 29.78
                               56.688 44.683 29.510 1.00 30.49
    ATOM 1893 N GLU 403
                               55.646 43.671 29.453 1.00 32.60
    ATOM 1894 CA GLU 403
                               54.562 44.094 28.469 1.00 37.01
    ATOM 1895 CB GLU 403
                               53.329 43.218 28.520 1.00 44.01
40
    ATOM 1896 CG GLU 403
                                52.263 43.632 27.523 1.00 48.50
    ATOM 1897 CD GLU 403
                                52.516 44.525 26.677 1.00 49.66
    ATOM 1898 OE1 GLU 403
                                51.157 43.050 27.594 1.00 53.06
    ATOM 1899 OE2 GLU 403
                               56.083 42.237 29.151 1.00 32.03
    ATOM 1900 C GLU 403
                               55.627 41.304 29.816 1.00 32.58
    ATOM 1901 O GLU 403
45
                               56.955 42.078 28.159 0.50 31.51
                                                             ALTA
    ATOM 1902 N VAL 404
                              57.450 40.765 27.739 0.50 30.96
    ATOM 1903 CA VAL 404
                                                              ALTA
    ATOM 1904 CB VAL 404
                               58.108 40.849 26.333 0.50 30.32
                                                              ALTA
    ATOM 1905 CG1 VAL 404 58.616 39.489 25.889 0.50 28.72
                                                              ALTA
    ATOM 1906 CG2 VAL 404
                               57.115 41.388 25.328 0.50 31.67
                                                              ALTA
50
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ATOM 1907 C VAL 404
                               58.465 40.149 28.696 0.50 30.45
                                                              ALTA
                               58.549 38.926 28.822 0.50 30.10
                                                              ALTA
    ATOM 1908 O VAL 404
    ATOM 1909 N PHE 405
                               59.224 41.002 29.369 1.00 30.16
                                60.266 40.549 30.263 1.00 30.65
    ATOM 1910 CA PHE 405
                                61.577 41.221 29.863 1.00 28.92
    ATOM 1911 CB PHE 405
    ATOM 1912 CG PHE 405
                                62.062 40.834 28.493 1.00 26.31
                                62,342 41.804 27.543 1.00 25.72
    ATOM 1913 CD1 PHE 405
                                62.269 39.500 28.166 1.00 25.92
    ATOM 1914 CD2 PHE 405
                                62.827 41.456 26.278 1.00 26.78
    ATOM 1915 CE1 PHE 405
                                62.752 39.139 26.910 1.00 25.39
    ATOM 1916 CE2 PHE 405
10
                                63.034 40.122 25.962 1.00 24.39
    ATOM 1917 CZ PHE 405
    ATOM 1918 C PHE 405
                               60.011 40.674 31.771 1.00 32.10
                               60.903 40.237 32.533 1.00 33.88
    ATOM 1919 O PHE 405
                                 58.936 41.169 32.188 1.00 34.95
    ATOM 1920 OXT PHE 405
                               67.542 37.066 11.311 1.00 26.83
15
    ATOM
             1 O1 HOH 501
    ATOM
             3 O1 HOH 502
                               68.713 41.227 12.821 1.00 23.42
             2 O1 HOH 503
                               64.446 40.325 12.123 1.00 22.84
    ATOM
                               62.236 39.752 15.941 1.00 17.97
    ATOM
             4 O1 HOH 504
             5 O1 HOH 505
                              48,732 20.137 5.515 1.00 50.48
    ATOM
                               47.365 21.522 3.716 1.00 53.40
20
    ATOM
             6 O1 HOH 506
                               50.211 23.203 7.900 1.00 32.66
             7 O1 HOH 507
    ATOM
             8 O1 HOH 508
                               51.043 20.258 8.253 1.00 21.81
    ATOM
                               48.225 18.176 7.905 1.00 38.96
             9 O1 HOH 509
     ATOM
                               49.569 20.871 11.586 1.00 32.97
             10 O1 HOH 510
     ATOM
    ATOM
             11 O1 HOH 511
                               53.732 17.159 10.856 1.00 47.20
25
                               56.201 16.223 12.164 1.00 18.50
    ATOM
             12 O1 HOH 512
                               56.653 12.298 10.528 1.00 27.71
             13 O1 HOH 513
    ATOM
                               58.661 10.694 9.014 1.00 46.73
             14 O1 HOH 514
     ATOM
                               62.950 10.692 11.952 1.00 43.05
     ATOM
             15 O1 HOH 515
             16 O1 HOH 516
                               66.411 11.552 10.897 1.00 37.36
30
     ATOM
                               68.949 13.188 12.029 1.00 39.28
             17 O1 HOH 517
     ATOM
                               71.997 15.171 8.362 1.00 49.69
     ATOM
             18 O1 HOH 518
             19 O1 HOH 519
                               71.946 17.928 6.743 1.00 24.50
     ATOM
                               75.117 15.684 9.377 1.00 35.98
     ATOM
             20 O1 HOH 520
                               76.677 12.815 10.294 1.00 49.33
             21 O1 HOH 521
35
     ATOM
                               81.421 15.415 15.139 1.00 46.74
     ATOM
             22 O1 HOH 522
             23 O1 HOH 523
                               78.784 21.696 17.564 1.00 49.01
     ATOM
                               79.954 24.822 17.152 1.00 42.91
             24 O1 HOH 524
     ATOM
     ATOM
             25 O1 HOH 525
                               82.199 30.253 18.821 1.00 40.27
                               82.862 33.444 21.988 1.00 46.81
             26 O1 HOH 526
     ATOM
40
                               76.608 30.793 23.452 1.00 46.22
     ATOM
             27 O1 HOH 527
                               74.726 30.483 25.469 1.00 43.76
     ATOM
             28 O1 HOH 528
     ATOM
             29 O1 HOH 529
                               77.059 28.762 20.900 1.00 33.67
                               75.935 33.279 12.269 1.00 25.26
             30 O1 HOH 530
     ATOM
                               77.402 34.447 10.087 1.00 37.04
             31 O1 HOH 531
     ATOM
                               74.054 29.941 9.998 1.00 26.86
     ATOM
             32 O1 HOH 532
                               69.544 32.658 7.572 1.00 40.34
     ATOM
             33 O1 HOH 533
                               66.709 33.618 8.477 1.00 20.63
             34 O1 HOH 534
     ATOM
                               68.073 35.828 8.931 1.00 23.99
             35 O1 HOH 535
     ATOM
                               61.865 45.643 14.011 1.00 40.43
50
     ATOM
             36 O1 HOH 536
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	ATOM	37 O1 HOH	537	63.662 46.881 15.670 1.00 28.04
	ATOM	38 O1 HOH		63.391 49.310 13.883 1.00 39.59
	ATOM	39 O1 HOH		63.491 50.570 10.631 1.00 52.34
		40 O1 HOH		64.592 46.849 10.299 1.00 26.63
5	ATOM ATOM	40 O1 HOH		55.575 41.632 10.980 1.00 38.06
)		41 O1 HOH		51.631 42.062 17.343 1.00 45.99
	ATOM	42 O1 HOH		52.755 43.156 20.209 1.00 34.17
	ATOM	44 O1 HOH		57.061 49.627 24.004 1.00 24.09
	ATOM			61.040 50.561 21.351 1.00 30.91
10	ATOM	45 O1 HOH 46 O1 HOH		
10	ATOM			
	ATOM	47 O1 HOH		63.371 58.813 29.014 1.00 59.25 57.934 52.905 31.175 1.00 40.12
	ATOM	48 O1 HOH		62.364 50.496 37.543 1.00 40.12
	ATOM	49 O1 HOH		62.256 49.704 40.891 1.00 54.18
1 0	ATOM	50 O1 HOH		61.994 46.430 40.384 1.00 43.84
15	ATOM	51 O1 HOH		
	ATOM	52 O1 HOH		63.675 44.459 39.268 1.00 44.73 58.405 43.920 33.936 1.00 42.88
	ATOM	53 O1 HOH		
	ATOM	54 O1 HOH		62.863 39.071 34.046 1.00 45.07 64.426 36.925 28.676 1.00 25.36
20	ATOM	55 O1 HOH		62.375 35.807 26.610 1.00 21.14
20	ATOM	56 O1 HOH		63.684 33.760 25.609 1.00 33.03
	ATOM	57 O1 HOH		61.542 29.906 24.568 1.00 57.37
	ATOM	58 O1 HOH		
	ATOM	59 O1 HOH		
25	ATOM	60 O1 HOH		
25	ATOM	61 O1 HOH		
	ATOM	62 O1 HOH		
	ATOM	63 O1 HOH		
	ATOM	64 O1 HOH		
20	ATOM	65 O1 HOH		
30	ATOM	66 O1 HOH		61.577 18.167 23.386 1.00 65.08 61.022 22.649 25.573 1.00 48.85
	ATOM	67 O1 HOH		
	ATOM	68 O1 HOH		57.919 21.446 25.147 1.00 43.39 59.435 20.179 28.543 1.00 51.41
	ATOM	69 O1 HOH		••••
2.5	ATOM	70 O1 HOH		53.860 23.216 30.984 1.00 50.28
35	ATOM	71 O1 HOH		52.825 24.880 32.696 1.00 43.96
	ATOM	72 O1 HOH		48.228 29.683 30.486 1.00 44.51
	ATOM	73 O1 HOH		48.925 34.467 30.521 1.00 36.28
	ATOM	74 O1 HOH		50.766 40.547 29.178 1.00 51.45
40	ATOM	75 O1 HOH		57.058 32.490 30.420 1.00 31.03
40	ATOM	76 O1 HOH		58.075 29.544 24.664 1.00 19.54
	ATOM	77 O1 HOH		47.451 19.292 28.703 1.00 33.04
	ATOM	78 O1 HOH		53.120 15.471 17.478 1.00 35.68
	ATOM	79 O1 HOH		55.101 14.146 16.095 1.00 50.46
	ATOM	80 O1 HOH		53.726 14.016 9.059 1.00 41.44
45	ATOM	81 O1 HOH		57.223 13.820 1.435 1.00 48.31
	ATOM	82 O1 HOH		61.169 15.688 0.210 1.00 17.60
	ATOM	83 O1 HOH		67.411 16.019 -0.314 1.00 23.93
	ATOM	84 O1 HOH		67.033 17.221 -2.796 1.00 26.21
	ATOM	85 O1 HOH		69.893 19.520 -1.582 1.00 59.67
50	ATOM	86 O1 HOH	586	68.489 22.464 0.350 1.00 37.85

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65.794 23.354 0.823 1.00 27.38
     ATOM
             87 O1 HOH 587
                               67.550 26.810 0.937 1.00 37.18
             88 O1 HOH 588
    ATOM
                               64.646 28.208 3.323 1.00 36.74
     ATOM
             89 O1 HOH 589
             90 O1 HOH 590
                               67.215 31.103 3.174 1.00 30.29
     ATOM
                               64.164 35.667 6.220 1.00 39.72
     ATOM
             91 O1 HOH 591
5
                               62.810 37.518 4.836 1.00 48.48
     ATOM
             92 O1 HOH 592
             93 O1 HOH 593
                               68.105 36.898 6.110 1.00 58.00
    ATOM
                               57.390 37.485 2.631 1.00 37.29
             94 O1 HOH 594
     ATOM
                               53.088 36.068 3.949 1.00 50.10
             95 O1 HOH 595
     ATOM
                               52,974 34.676 6.758 1.00 42.52
             96 O1 HOH 596
    ATOM
10
                               58.581 31.465 2.076 1.00 32.18
     ATOM
             97 O1 HOH 597
                               52.786 23.277 1.357 1.00 28.98
     ATOM
             98 O1 HOH 598
                               47.501 26.551 7.672 1.00 47.83
    ATOM
             99 O1 HOH 599
                                46,411 35.754 14.049 1.00 53.46
            100 O1 HOH 600
     ATOM
                                63.514 14.944 15.842 1.00 55.02
            101 O1 HOH 601
15
     ATOM
                                67.943 11.792 3.438 1.00 61.21
     ATOM ·
            102 O1 HOH 602
                                62.232 9.378 3.311 1.00 35.65
     ATOM
            103 O1 HOH 603
                                76.734 22.468 5.002 1.00 42.56
            104 O1 HOH 604
     ATOM
                                83.589 28.967 9.626 1.00 50.64
     ATOM
            105 O1 HOH 605
                                82.807 43.437 17.940 1.00 39.28
            106 O1 HOH 606
20
     ATOM
                                83.882 45.673 20.638 1.00 41.64
     ATOM
            107 O1 HOH 607
            108 O1 HOH 608
                                80.215 41.021 23.441 1.00 43.16
     ATOM
                                79.459 46.296 31.165 1.00 32.40
            109 O1 HOH 609
     ATOM
                                81.880 47.681 33.923 1.00 46.96
            110 O1 HOH 610
     ATOM
                                75.594 46.142 30.384 1.00 28.64
25
     ATOM 111 O1 HOH 611
                                77.118 40.568 32.575 1.00 34.21
     ATOM 112 O1 HOH 612
                                73.563 41.750 36.926 1.00 26.07
     ATOM 113 O1 HOH 613
                                75.955 56.565 28.863 1.00 46.31
     ATOM 114 O1 HOH 614
                                79.915 59.136 15.809 1.00 50.81
     ATOM 115 O1 HOH 615
                                77.390 52.542 8.816 1.00 34.34
30
     ATOM 116 O1 HOH 616
                                72.726 25.005 29.671 1.00 62.84
     ATOM 117 O1 HOH 617
                                52.664 40.106 24.800 1.00 46.39
     ATOM 2038 C ACY 701
                                53.721 39.649 24.298 1.00 47.12
     ATOM 2039 O ACY 701
                                 51.652 40.521 24.172 1.00 46.96
     ATOM 2040 OXT ACY 701
                                 52.600 40.162 26.329 1.00 45.99
     ATOM 2041 CH3 ACY 701
35
                              66.961 42.243 18.491 1.00 22.34
     ATOM 2050 C1 T3
                          1
                              68.748 43.593 23.015 1.00 21.84
     ATOM 2051 C2 T3
                          1
     ATOM 2052 C3 T3
                              66.873 43.557 18.970 1.00 23.43
                         1
                              69.252 44.540 23.871 1.00 22.31
     ATOM 2053 C4 T3
                              67.638 43.989 20.011 1.00 24.83
40
     ATOM 2054 C5 T3
                          1
     ATOM 2055 C6 T3
                              68.851 44.553 25.178 1.00 25.16
                          1
                              68.541 43.108 20.632 1.00 24.65
     ATOM 2056 C7 T3
                          1
                              67.895 43.567 25.639 1.00 21.93
     ATOM 2057 C8 T3
                              68.665 41.792 20.183 1.00 25.09
     ATOM 2058 C9 T3
                              67.427 42.654 24.733 1.00 23.66
     ATOM 2059 C10 T3
45
                          1
                              67.878 41.380 19.117 1.00 23.12
     ATOM 2060 C11 T3
                          1
                              67.829 42.624 23.384 1.00 19.67
     ATOM 2061 C12 T3
                          1
                              66.055 41.788 17.371 1.00 18.97
     ATOM 2062 C13 T3
                          1
                              66.721 40.956 16.295 1.00 19.32
     ATOM 2063 C15 T3
                              65.901 40.829 15.051 1.00 19.02
     ATOM 2064 C17 T3
                          1
50
```

ATOM 2065 II T3 67.393 45.986 20.621 1.00 25.29 ATOM 2066 I2 T3 69.483 46.066 26.432 1.00 26.49 1 ATOM 2067 I3 T3 70.019 40.450 20.975 1.00 25.67 1 68.131 41.337 16.037 1.00 15.12 ATOM 2068 N1 T3 1 67.542 43.587 26.966 1.00 21.79 ATOM 2069 O1 T3 1 69.259 43.600 21.682 1.00 22.05 ATOM 2070 O2 T3 1 66.504 40.852 13.963 1.00 20.38 ATOM 2071 O3 T3 1 64.675 40.731 15.192 1.00 20.16 ATOM 2072 O4 T3 1 **END**

APPENDIX 7

TRBTRIAC.PDB

REMARK TR-beta Triac Full length numbering

REMARK refinement resolution: 100 - 2.9 A r= 0.273258 free_r= 0.333794

5 REMARK wa= 5.78307

REMARK target= mlf cycles= 1 steps= 25

REMARK a= 68.72 b= 68.72 c= 130.092 alpha= 90 beta= 90 gamma= 120

REMARK ncs= none

REMARK initial B-factor correction: "none"

10 REMARK ALA 199 to ALA 201 from His-tag

REMARK

REMARK Four cacodylate-modified cysteines (CYA)

REMARK Cys294, Cys298, Cys388, Cys434

REMARK cacodylate modeled as single arsenic atom

15 REMARK

REMARK side chain of certain residues modeled as ALA due to poor density;

REMARK however, residue name reflects true residue for clarity

REMARK

REMARK amino acid sequence confirmed,

20 REMARK differing from that reported by Weinberger et. al.

REMARK in the following codons:

REMARK 243 Pro - Arg

REMARK 337 lle - Thr

REMARK 451 Leu - Phe

25 REMARK as reported by Sakurai et. al.

REMARK note also correction of initiation codon,

REMARK yielding a polypeptide of 461 amino acids

JRNL AUTH A.SAKURAI, A.NAKAI, L.J.DEGROOT

JRNL TITL STRUCTURAL ANALYSIS OF HUMAN THYROID HORMONE

30 RECEPTOR

JRNL TITL2 BETA GENE

JRNL REF MOL.CELL.ENDO. V.71 1990

JRNL AUTH

C.WEINBERGER,

C.C.THOMPSON, R. LEBO, D. J. GRUOL, R.M. EVANS

JRNL TITL THE C-ERB-A GENE ENCODES A THYROID HORMONE RECEPTOR

JRNL REF NATURE

V.324 6098 1986

ATOM	1 CB ALA 199	31.247 28.289 43.613 1.00 71.30	PROT
ATOM	2 C ALA 199	32.916 26.485 44.170 1.00 68.99	PROT
ATOM	3 O ALA 199	33.485 25.410 43.976 1.00 63.84	PROT
ATOM	4 N ALA 199	30.462 25.993 44.096 1.00 75.00	PROT
ATOM	5 CA ALA 199	31.571 26.795 43.497 1.00 73.24	PROT
ATOM	6 N ALA 200	33.419 27.432 44.958 1.00 73.81	PROT
ATOM	7 CA ALA 200	34.686 27.251 45.658 1.00 67.87	PROT
ATOM	8 CB ALA 200	35.182 28.583 46.203 1.00 62.83	PROT
ATOM	9 C ALA 200	34.539 26.239 46.791 1.00 63.23	PROT
ATOM	10 O ALA 200	35.486 25.986 47.534 1.00 59.14	PROT
	ATOM ATOM ATOM ATOM ATOM ATOM ATOM	ATOM 2 C ALA 199 ATOM 3 O ALA 199 ATOM 4 N ALA 199 ATOM 5 CA ALA 199 ATOM 6 N ALA 200 ATOM 7 CA ALA 200 ATOM 8 CB ALA 200 ATOM 9 C ALA 200	ATOM 2 C ALA 199 32.916 26.485 44.170 1.00 68.99 ATOM 3 O ALA 199 33.485 25.410 43.976 1.00 63.84 ATOM 4 N ALA 199 30.462 25.993 44.096 1.00 75.00 ATOM 5 CA ALA 199 31.571 26.795 43.497 1.00 73.24 ATOM 6 N ALA 200 33.419 27.432 44.958 1.00 73.81 ATOM 7 CA ALA 200 34.686 27.251 45.658 1.00 67.87 ATOM 8 CB ALA 200 34.539 26.239 46.791 1.00 63.23

	ATOM ATOM	11 N ALA 201 12 CA ALA 201	33.345 25.670 46.932 1.00 56.98 33.117 24.664 47.957 1.00 51.46	PROT PROT
	ATOM	13 CB ALA 201	31.776 23.992 47.744 1.00 40.35	PROT
	ATOM	14 C ALA 201	34.248 23.662 47.762 1.00 53.15	PROT
5	ATOM	15 O ALA 201	34.624 22.938 48.679 1.00 54.90	PROT
	ATOM	16 N GLU 202	34.789 23.645 46.546 1.00 44.13	PROT
	ATOM	17 CA GLU 202	35.891 22.767 46.190 1.00 37.47	PROT
	ATOM	18 CB GLU 202	36.086 22.760 44.671 1.00 37.74	PROT
	ATOM	19 CG GLU 202	37.060 21.702 44.173 1.00 57.14	PROT
10	ATOM	20 CD GLU 202	36.457 20.303 44.140 1.00 61.74	PROT
	ATOM	21 OE1 GLU 202	35.211 20.175 44.133 1.00 63.81	PROT
	ATOM	22 OE2 GLU 202	37.236 19.327 44.115 1.00 65.54	PROT
	ATOM	23 C GLU 202	37.156 23.266 46.878 1.00 35.54	PROT
	ATOM	24 O GLU 202	37.874 22.492 47.510 1.00 32.70	PROT
15	ATOM	25 N GLU 203	37.415 24.566 46.755 1.00 31.79	PROT
	ATOM	26 CA GLU 203	38.588 25.188 47.366 1.00 33.63	PROT
	ATOM	27 CB GLU 203	38.603 26.683 47.079 1.00 28.28	PROT
	ATOM	28 C GLU 203	38.588 24.948 48.869 1.00 33.86	PROT
	ATOM	29 O GLU 203	39.644 24.818 49.485 1.00 33.10	PROT
20	ATOM	30 N LEU 204	37.393 24.898 49.451 1.00 34.15	PROT
	ATOM	31 CA LEU 204	37.244 24.650 50.876 1.00 33.22	PROT
	ATOM	32 CB LEU 204	35.853 25.081 51.353 1.00 30.47	PROT
	ATOM	33 CG LEU 204	35.567 25.083 52.862 1.00 23.17	PROT
	ATOM	34 CD1 LEU 204	35.904 26.439 53.443 1.00 5.41	PROT
25	ATOM	35 CD2 LEU 204	34.106 24.748 53.111 1.00 12.70	PROT
	ATOM	36 C LEU 204	37.424 23.156 51.100 1.00 40.17	PROT
	ATOM	37 O LEU 204	38.219 22.736 51.951 1.00 45.33	PROT
	ATOM	38 N GLN 205	36.682 22.360 50.329 1.00 43.86	PROT PROT
20	ATOM	39 CA GLN 205	36.754 20.899 50.415 1.00 43.96 36.089 20.261 49.184 1.00 45.56	PROT
30	ATOM	40 CB GLN 205	34.562 20.195 49.245 1.00 42.39	PROT
	ATOM	41 CG GLN 205 42 CD GLN 205	34.022 18.775 49.159 1.00 42.39	PROT
	ATOM ATOM	42 CD GLN 205 43 OE1 GLN 205	33.258 18.444 48.252 1.00 38.84	PROT
	ATOM	44 NE2 GLN 205	34.412 17.932 50.109 1.00 37.95	PROT
35	ATOM	45 C GLN 205	38.224 20.482 50.483 1.00 42.39	PROT
22	ATOM	46 O GLN 205	38.630 19.702 51.355 1.00 36.27	PROT
	ATOM	47 N LYS 206	39.014 21.015 49.553 1.00 42.37	PROT
	ATOM		40.440 20.729 49.505 1.00 44.40	PROT
	ATOM	49 CB LYS 206	41.110 21.531 48.385 1.00 38.73	PROT
40	ATOM	50 C LYS 206	41.024 21.118 50.853 1.00 42.36	PROT
	ATOM	51 O LYS 206	41.550 20.271 51.570 1.00 46.93	PROT
	ATOM	52 N SER 207	40.913 22.401 51.192 1.00 34.68	PROT
	ATOM	53 CA SER 207	41.415 22.933 52.455 1.00 29.43	PROT
	ATOM	54 CB SER 207	40.690 24.228 52.791 1.00 24.63	PROT
45	ATOM	55 OG SER 207	41.327 25.332 52.173 1.00 36.56	PROT
	ATOM	56 C SER 207	41.254 21.958 53.614 1.00 29.20	PROT
	ATOM	57 O SER 207	42.223 21.623 54.293 1.00 31.01	PROT
	ATOM	58 N ILE 208	40.028 21.504 53.841 1.00 22.55	PROT
	ATOM	59 CA ILE 208	39.777 20.568 54.928 1.00 27.93	PROT
50	ATOM	60 CB ILE 208	38.267 20.216 55.027 1.00 39.85	PROT

	ATOM ATOM	61 CG2 ILE 208 62 CG1 ILE 208	38.062 18.895 55.769 1.00 32.13 37.528 21.340 55.753 1.00 37.63	PROT PROT
	ATOM	63 CD1 ILE 208	36.788 22.296 54.827 1.00 41.47	PROT
	ATOM	64 C ILE 208		PROT
5	ATOM	65 O ILE 208		PROT
	ATOM	66 N GLY 209	40.928 19.002 53.475 1.00 35.05	PROT
	ATOM	67 CA GLY 209	41.698 17.809 53.181 1.00 31.94	PROT
	ATOM	68 C GLY 209	40.826 16.695 52.643 1.00 28.66	PROT
	ATOM	69 O GLY 209	41.257 15.553 52.532 1.00 19.46	PROT
10	ATOM	70 N HIS 210	39.586 17.021 52.313 1.00 20.47	PROT
	ATOM	71 CA HIS 210	38.684 16.018 51.774 1.00 26.99	PROT
	ATOM	72 CB HIS 210	37.240 16.451 52.012 1.00 37.16	PROT
	ATOM	73 C HIS 210		PROT
	ATOM	74 O HIS 210	39.328 16.741 49.550 1.00 34.08	PROT
15	ATOM	75 N LYS 211	38.807 14.566 49.805 1.00 16.50	PROT
	ATOM	76 CA LYS 211	39.019 14.206 48.403 1.00 5.57	PROT
	ATOM	77 CB LYS 211	39.932 12.981 48.295 1.00 5.67	PROT
	ATOM	78 CG LYS 211	41.370 13.208 48.742 1.00 7.30	PROT
	ATOM	79 CD LYS 211	41.873 14.594 48.347 1.00 14.34	PROT
20	ATOM	80 CE LYS 211	43.339 14.556 47.897 1.00 29.48	PROT
	ATOM	81 NZ LYS 211	43.777 15.851 47.262 1.00 33.43	PROT
	ATOM	82 C LYS 211		PROT
	ATOM	83 O LYS 211	37.176 12.741 48.039 1.00 6.57	PROT
	ATOM	84 N PRO 212	36.983 14.813 47.208 1.00 2.00	PROT
25	ATOM	85 CD PRO 212	37.472 16.156 46.846 1.00 10.43	PROT
	ATOM	86 CA PRO 212	35.642 14.542 46.689 1.00 2.05	PROT.
	ATOM	87 CB PRO 212	35.088 15.928 46.341 1.00 10.09	PROT
	ATOM	88 CG PRO 212	36.240 16.888 46.422 1.00 8.43	PROT
	ATOM	89 C PRO 212	35.523 13.578 45.520 1.00 2.00	PROT
30	ATOM	90 O PRO 212	36.344 13.554 44.611 1.00 6.04	PROT
	ATOM	91 N GLU 213	34.476 12.773 45.577 1.00 2.68	PROT
	ATOM	92 CA GLU 213	34.181 11.817 44.542 1.00 6.81	PROT
	ATOM	93 CB GLU 213	33.539 10.594 45.173 1.00 7.20	PROT
	ATOM	94 CG GLU 213	34.222 10.232 46.462 1.00 15.33	PROT
35	ATOM	95 CD GLU 213	34.293 8.743 46.689 1.00 21.36	PROT
	ATOM	96 OE1 GLU 213	33.334 8.051 46.290 1.00 29.32	PROT
	ATOM	97 OE2 GLU 213	35.301 8.265 47.268 1.00 28.50	PROT
	ATOM	98 C GLU 213	33.229 12.543 43.584 1.00 12.00	PROT
	ATOM	99 O GLU 213	32.693 13.599 43.926 1.00 19.02	PROT
40	ATOM	100 N PRO 214	33.011 11.985 42.375 1.00 25.74	PROT
	ATOM	101 CD PRO 214	33.592 10.692 41.973 1.00 28.98	PROT
	ATOM	102 CA PRO 214	32.145 12.536 41.322 1.00 23.38	PROT
	ATOM	103 CB PRO 214	32.180 11.476 40.232 1.00 18.01	PROT
	ATOM	104 CG PRO 214	33.376 10.665 40.514 1.00 27.50	PROT
45	ATOM	105 C PRO 214	30.715 12.828 41.734 1.00 25.02	PROT
	ATOM	106 O PRO 214	30.069 11.986 42.355 1.00 31.17	PROT
	ATOM	107 N THR 215	30.211 14.009 41.377 1.00 19.56	PROT
	ATOM	108 CA THR 215		PROT
	ATOM	109 CB THR 215		PROT
50	ATOM	110 OG1 THR 215	27.939 16.038 40.234 1.00 40.19	PROT

	ATOM	111 CG2 THR 215	29.805 16.659 41.640 1.00 30.81	PROT
	ATOM	112 C THR 215	27.899 13.562 40.805 1.00 22.14	PROT
	ATOM	113 O THR 215	28.357 12.905 39.883 1.00 27.52	PROT
	ATOM	114 N ASP 216	26.599 13.617 41.072 1.00 35.65	PROT
5	ATOM	115 CA ASP 216	25.631 12.890 40.258 1.00 41.16	PROT
	ATOM	116 CB ASP 216	24.219 13.091 40.810 1.00 38.17	PROT
	ATOM	117 C ASP 216	25.714 13.370 38.810 1.00 40.44	PROT
	ATOM	118 O ASP 216	25.683 12.569 37.874 1.00 38.26	PROT
	ATOM	119 N GLU 217	25.832 14.682 38.635 1.00 40.14	PROT
10	ATOM	120 CA GLU 217	25.932 15.275 37.305 1.00 38.89	PROT
	ATOM	121 CB GLU 217	25.883 16.796 37.413 1.00 29.95	PROT
	ATOM	122 C GLU 217	27.231 14.829 36.619 1.00 39.44	PROT
	ATOM	123 O GLU 217	27.245 14.525 35.425 1.00 40.08	PROT
	ATOM	124 N GLU 218	28.319 14.794 37.384 1.00 34.92	PROT
15	ATOM	125 CA GLU 218	29.615 14.370 36.871 1.00 23.70	PROT
	ATOM	126 CB GLU 218	30.698 14.606 37.924 1.00 18.47	PROT
	ATOM	127 CG GLU 218	30.990 16.067 38.198 1.00 15.66	PROT
	ATOM	128 CD GLU 218	32.085 16.264 39.231 1.00 26.88	PROT
	ATOM	129 OE1 GLU 218	32.164 15.458 40.191 1.00 25.07	PROT
20	ATOM	130 OE2 GLU 218	32.864 17.232 39.078 1.00 33.79	PROT
	ATOM	131 C GLU 218	29.589 12.892 36.491 1.00 21.05	PROT
	ATOM	132 O GLU 218	30.182 12.490 35.495 1.00 24.30	PROT
	ATOM	133 N TRP 219	28.907 12.080 37.288 1.00 13.98	PROT
0.5	ATOM	134 CA TRP 219	28.829 10.660 37.000 1.00 17.30	PROT
25	ATOM	135 CB TRP 219	28.052 9.921 38.089 1.00 16.27	PROT
	ATOM	136 CG TRP 219	28.890 9.520 39.277 1.00 31.14 29.984 8.585 39.296 1.00 36.40	PROT PROT
	ATOM	137 CD2 TRP 219 138 CE2 TRP 219	30.476 8.547 40.621 1.00 29.24	PROT
	ATOM	138 CE2 TRP 219 139 CE3 TRP 219	30.595 7.781 38.323 1.00 41.61	PROT
30	ATOM ATOM	140 CD1 TRP 219	28.771 9.988 40.551 1.00 28.69	PROT
30	ATOM	140 CDI TRP 219	29.718 9.411 41.362 1.00 35.01	PROT
	ATOM	141 NEI TRI 219	31.552 7.737 41.004 1.00 30.89	PROT
	ATOM	142 CZ2 TRI 219	31.673 6.969 38.707 1.00 45.72	PROT
	ATOM	144 CH2 TRP 219	32.137 6.958 40.038 1.00 35.17	PROT
35	ATOM	145 C TRP 219	28.125 10.500 35.660 1.00 20.83	PROT
<i></i>	ATOM	146 O TRP 219	28.467 9.616 34.865 1.00 31.36	PROT
	ATOM	147 N GLU 220	27.143 11.364 35.412 1.00 30.53	PROT
	ATOM	148 CA GLU 220	26.400 11.323 34.159 1.00 33.95	PROT
	ATOM	149 CB GLU 220	25.237 12.318 34.201 1.00 22.17	PROT
40	ATOM	150 C GLU 220	27.356 11.658 33.013 1.00 34.66	PROT
•	ATOM	151 O GLU 220	27.233 11.134 31.900 1.00 43.86	PROT
	ATOM	152 N LEU 221	28.320 12.528 33.297 1.00 22.60	PROT
	ATOM	153 CA LEU 221	29.305 12.926 32.304 1.00 17.18	PROT
	ATOM	154 CB LEU 221	29.995 14.219 32.743 1.00 11.03	PROT
45	ATOM	155 CG LEU 221	31.078 14.824 31.850 1.00 5.17	PROT
	ATOM	156 CD1 LEU 221	30.756 14.569 30.415 1.00 6.41	PROT
	ATOM	157 CD2 LEU 221	31.181 16.305 32.092 1.00 10.65	PROT
	ATOM	158 C LEU 221	30.344 11.817 32.122 1.00 22.25	PROT
	ATOM	159 O LEU 221	30.759 11.521 31.002 1.00 18.99	PROT
50	ATOM	160 N ILE 222	30.754 11.198 33.228 1.00 20.74	PROT

	ATOM	161 CA ILE 222 31.744 10.136 33.177 1.00 12.88	PROT
	ATOM	162 CB ILE 222 32.115 9.662 34.587 1.00 12.96	PROT
	ATOM	163 CG2 ILE 222 33.030 8.468 34.515 1.00 2.00	PROT
	ATOM	164 CG1 ILE 222 32.811 10.796 35.332 1.00 16.50	PROT
5	ATOM	165 CD1 ILE 222 33.625 10.351 36.511 1.00 15.90	PROT
	ATOM	166 C ILE 222 31.241 8.958 32.363 1.00 17.72	PROT
	ATOM	167 O ILE 222 32.001 8.363 31.594 1.00 16.59	PROT
	ATOM	168 N LYS 223 29.966 8.618 32.530 1.00 33.88	PROT
	ATOM	169 CA LYS 223 29.371 7.503 31.795 1.00 39.02	PROT
10	ATOM	170 CB LYS 223 27.908 7.307 32.224 1.00 40.29	PROT
	ATOM	171 C LYS 223 29.444 7.779 30.293 1.00 39.14	PROT
	ATOM	172 O LYS 223 29.949 6.963 29.517 1.00 32.99	PROT
	ATOM	173 N THR 224 28.936 8.942 29.897 1.00 27.19	PROT
	ATOM	174 CA THR 224 28.929 9.363 28.498 1.00 25.75	PROT
15	ATOM	175 CB THR 224 28.440 10.817 28.407 1.00 22.51	PROT
	ATOM	176 OG1 THR 224 27.018 10.837 28.568 1.00 35.46	PROT
	ATOM	177 CG2 THR 224 28.799 11.436 27.083 1.00 15.53	PROT
	ATOM	178 C THR 224 30.307 9.235 27.833 1.00 22.31	PROT
	ATOM	179 O THR 224 30.480 8.517 26.843 1.00 27.13	PROT
20	ATOM	180 N VAL 225 31.287 9.936 28.386 1.00 17.87	PROT
	ATOM	181 CA VAL 225 32.635 9.906 27.854 1.00 17.07	PROT
	ATOM	182 CB VAL 225 33.559 10.759 28.720 1.00 16.86	PROT
	ATOM	183 CG1 VAL 225 34.845 11.064 27.973 1.00 26.54	PROT
	ATOM	184 CG2 VAL 225 32.854 12.057 29.075 1.00 24.46	PROT
25	ATOM	185 C VAL 225 33.169 8.486 27.793 1.00 16.11	PROT
	ATOM	186 O VAL 225 33.683 8.042 26.763 1.00 12.75	PROT
	ATOM	187 N THR 226 33.040 7.769 28.900 1.00 12.23	PROT
	ATOM	188 CA THR 226 33.520 6.400 28.951 1.00 12.34	PROT
	ATOM	189 CB THR 226 33.175 5.747 30.271 1.00 17.01	PROT
30	ATOM	190 OG1 THR 226 33.715 6.536 31.342 1.00 6.78	PROT
	ATOM	191 CG2 THR 226 33.739 4.324 30.307 1.00 2.00	PROT
	ATOM	192 C THR 226 32.909 5.581 27.837 1.00 14.82	PROT
	ATOM	193 O THR 226 33.623 4.953 27.061 1.00 20.90	PROT
	ATOM	194 N GLU 227 31.582 5.588 27.758 1.00 22.90	PROT
35	ATOM	195 CA GLU 227 30.886 4.849 26.714 1.00 22.63	PROT
	ATOM	196 CB GLU 227 29.417 5.248 26.678 1.00 20.14	PROT
	ATOM	197 C GLU 227 31.556 5.173 25.386 1.00 21.74	PROT
	ATOM	198 O GLU 227 32.057 4.283 24.700 1.00 24.42	PROT
	ATOM	199 N ALA 228 31.590 6.460 25.050 1.00 13.26	PROT
40	ATOM	200 CA ALA 228 32.196 6.928 23.800 1.00 22.76	PROT
	ATOM	201 CB ALA 228 32.267 8.450 23.785 1.00 22.50	PROT
	ATOM	202 C ALA 228 33.584 6.358 23.538 1.00 19.19	PROT
	ATOM	203 O ALA 228 33.913 6.003 22.408 1.00 17.19	PROT
	ATOM	204 N HIS 229 34.408 6.290 24.573 1.00 20.11	PROT
45	ATOM	205 CA HIS 229 35.741 5.756 24.389 1.00 18.68	PROT
	ATOM	206 CB HIS 229 36.537 5.819 25.686 1.00 10.37	PROT
	ATOM	207 CG HIS 229 37.894 5.201 25.586 1.00 2.00	PROT
	ATOM	208 CD2 HIS 229 38.524 4.299 26.376 1.00 7.61	PROT
	ATOM	209 ND1 HIS 229 38.780 5.517 24.582 1.00 3.78	PROT
50	ATOM	210 CE1 HIS 229 39.900 4.837 24.758 1.00 15.67	PROT

	ATOM	211 NE2 HIS 229	39.771 4.090 25.840 1.00 7.10	PROT
	ATOM	212 C HIS 229	35.637 4.316 23.940 1.00 21.45	PROT
	ATOM	213 O HIS 229	36.127 3.950 22.866 1.00 22.42	PROT
	ATOM	214 N VAL 230	34.983 3.505 24.762 1.00 21.64	PROT
5	ATOM	215 CA VAL 230	34.827 2.086 24.468 1.00 33.80	PROT
	ATOM	216 CB VAL 230	33.960 1.388 25.528 1.00 33.11	PROT
	ATOM	217 CG1 VAL 230	34.251 -0.106 25.515 1.00 33.80	PROT
	ATOM	218 CG2 VAL 230	34.228 1.985 26.896 1.00 26.54	PROT
	ATOM	219 C VAL 230	34.224 1.781 23.100 1.00 33.12	PROT
10	ATOM	220 O VAL 230	34.703 0.897 22.385 1.00 40.80	PROT
	ATOM	221 N ALA 231	33.170 2.507 22.746 1.00 36.22	PROT
	ATOM	222 CA ALA 231	32.497 2.298 21.471 1.00 36.24	PROT
	ATOM	223 CB ALA 231	31.318 3.255 21.343 1.00 18.90	PROT
	ATOM	224 C ALA 231	33.445 2.501 20.303 1.00 37.54	PROT
15	ATOM	225 O ALA 231	33.342 1.816 19.285 1.00 35.93	PROT
	ATOM	226 N THR 232	34.380 3.434 20.474 1.00 23.74	PROT
	ATOM	227 CA THR 232	35.329 3.789 19.432 1.00 15.54	PROT
	ATOM	228 CB THR 232	35.335 5.321 19.238 1.00 9.70	PROT
	ATOM	229 OG1 THR 232	35.733 5.949 20.460 1.00 16.73	PROT
20	ATOM	230 CG2 THR 232	33.942 5.828 18.891 1.00 2.00	PROT
	ATOM	231 C THR 232	36.758 3.309 19.670 1.00 19.86	PROT ·
	ATOM	232 O THR 232	37.695 3.854 19.094 1.00 15.31	PROT
	ATOM	233 N ASN 233	36.938 2.305 20.523 1.00 28.26	PROT
	ATOM	234 CA ASN 233	38.280 1.771 20.772 1.00 39.32	PROT
25	ATOM	235 CB ASN 233	38.435 1.343 22.234 1.00 47.14	PROT
	ATOM	236 CG ASN 233	39.804 1.689 22.801 1.00 54.02	PROT
	ATOM	237 OD1 ASN 233	40.633 2.303 22.128 1.00 60.36	PROT
	ATOM	238 ND2 ASN 233	40.045 1.296 24.045 1.00 48.67	PROT
	ATOM	239 C ASN 233	38.507 0.574 19.840 1.00 49.33	PROT
30	ATOM	240 O ASN 233	38.338 0.693 18.625 1.00 65.36	PROT
	ATOM	241 N ALA 234	38.877 -0.577 20.388 1.00 57.89	PROT
	ATOM	242 CA ALA 234	39.090 -1.752 19.552 1.00 57.22	PROT
	ATOM	243 CB ALA 234	40.372 -1.595 18.754 1.00 48.03	PROT
	ATOM	244 C ALA 234	39.141 -3.027 20.384 1.00 62.42	PROT
35	ATOM	245 O ALA 234	38.471 -3.073 21.440 1.00 56.93	PROT
	ATOM	246 OT ALA 234	39.853 -3.968 19.965 1.00 76.16	PROT
	ATOM	247 N TRP 239	41.987 -7.449 22.970 1.00 58.82	PROT
	ATOM	248 CA TRP 239	43.077 -6.886 22.154 1.00 51.37	PROT
	ATOM	249 CB TRP 239	43.325 -5.406 22.534 1.00 45.12	PROT
40	ATOM	250 CG TRP 239	44.193 -5.170 23.760 1.00 43.09	PROT
	ATOM	251 CD2 TRP 239	45.617 -5.037 23.793 1.00 32.36	PROT
	ATOM	252 CE2 TRP 239	45.990 -4.872 25.142 1.00 28.37	PROT
	ATOM	253 CE3 TRP 239	46.615 -5.049 22.813 1.00 40.79	PROT
	ATOM	254 CD1 TRP 239	43.773 -5.073 25.059 1.00 46.63	PROT
45	ATOM	255 NE1 TRP 239	44.847 -4.896 25.893 1.00 27.08	PROT
43	ATOM	256 CZ2 TRP 239	47.315 -4.717 25.535 1.00 35.48	PROT
	ATOM	257 CZ3 TRP 239	47.936 -4.896 23.204 1.00 40.18	PROT
	ATOM	257 CZ3 TRI 239 258 CH2 TRP 239	48.273 -4.733 24.554 1.00 49.93	PROT
	ATOM	259 C TRP 239	44.422 -7.623 22.063 1.00 49.76	PROT
50	ATOM	260 O TRP 239	44.944 -7.799 20.962 1.00 48.14	PROT
50	Y I OIM	200 O 110 239	17.777 -1.177 20.702 1.00 70.17	11(01

	ATOM	261 N LYS 240	44.975 -8.048 23.198 1.00 38.92	PROT
	ATOM	262 CA LYS 240	46.263 -8.735 23.232 1.00 37.29	PROT
	ATOM	263 CB LYS 240	46.572 -9.196 24.657 1.00 38.79	PROT
	ATOM	264 CG LYS 240	47.106 -8.099 25.571 1.00 38.43	PROT
5	ATOM	265 CD LYS 240	48.307 -8.584 26.370 1.00 35.71	PROT
	ATOM	266 CE LYS 240	48.631 -7.646 27.523 1.00 37.87	PROT
,	ATOM	267 NZ LYS 240	49.058 -8.377 28.750 1.00 28.85	PROT
	ATOM	268 C LYS 240	46.404 -9.914 22.269 1.00 42.18	PROT
	ATOM	269 O LYS 240	47.491 -10.132 21.732 1.00 45.89	PROT
10	ATOM	270 N GLN 241	45.331 -10.679 22.058 1.00 46.08	PROT
	ATOM	271 CA GLN 241	45.390 -11.816 21.133 1.00 45.02	PROT
	ATOM	272 CB GLN 241	44.575 -13.011 21.638 1.00 46.30	PROT
	ATOM	273 CG GLN 241	44.284 -13.018 23.116 1.00 60.38	PROT
	ATOM	274 CD GLN 241	42.828 -13.312 23.408 1.00 63.76	PROT
15	ATOM	275 OE1 GLN 241	42.154 -13.988 22.631 1.00 66.34	PROT
	ATOM	276 NE2 GLN 241	42.333 -12.801 24.531 1.00 69.18	PROT
	ATOM	277 C GLN 241	44.866 -11.405 19.764 1.00 45.77	PROT
	ATOM	278 O GLN 241	45.107 -12.085 18.765 1.00 51.18	PROT
	ATOM	279 N LYS 242	44.132 -10.300 19.723 1.00 42.04	PROT
20	ATOM	280 CA LYS 242	43.613 -9.794 18.464 1.00 48.33	PROT
	ATOM	281 CB LYS 242	42.498 -8.786 18.727 1.00 40.17	PROT
	ATOM	282 C LYS 242	44.796 -9.123 17.742 1.00 53.04	PROT
	ATOM	283 O LYS 242	44.709 -8.753 16.565 1.00 48.21	PROT
	ATOM	284 N ARG 243	45.906 -8.992 18.470 1.00 45.44	PROT
25	ATOM	285 CA ARG 243	47.128 -8.374 17.965 1.00 43.53	PROT
	ATOM	286 CB ARG 243	48.108 -8.135 19.118 1.00 40.21	PROT
	ATOM	287 C ARG 243	47.795 -9.220 16.892 1.00 45.96	PROT
	ATOM	288 O ARG 243	47.684 -10.443 16.894 1.00 50.22	PROT
	ATOM	289 N LYS 244	48.498 -8.551 15.982 1.00 52.12	PROT
30	ATOM	290 CA LYS 244	49.202 -9.202 14.879 1.00 45.30	PROT
	ATOM	291 CB LYS 244	48.466 -8.950 13.558 1.00 48.24	PROT
	ATOM	292 CG LYS 244	47.109 -9.631 13.446 1.00 53.78	PROT
	ATOM	293 CD LYS 244	46.835 -10.078 12.011 1.00 60.50	PROT
	ATOM	294 CE LYS 244	46.038 -9.030 11.241 1.00 61.03	PROT
35	ATOM	295 NZ LYS 244	45.455 -7.997 12.146 1.00 55.25	PROT
	ATOM	296 C LYS 244	50.616 -8.641 14.786 1.00 40.33	PROT
	ATOM	297 O LYS 244	50.849 -7.629 14.125 1.00 36.07	PROT
	ATOM	298 N PHE 245	51.556 -9.312 15.445 1.00 27.87	PROT
	ATOM	299 CA PHE 245	52.949 -8.885 15.461 1.00 30.61	PROT
40	ATOM	300 CB PHE 245	53.784 -9.887 16.253 1.00 20.28	PROT
	ATOM	301 CG PHE 245	53.454 -9.922 17.713 1.00 37.23	PROT
	ATOM	302 CD1 PHE 245	52.636 -10.917 18.234 1.00 40.93	PROT
	ATOM	303 CD2 PHE 245	53.958 -8.959 18.577 1.00 41.60	PROT
	ATOM	304 CE1 PHE 245	52.326 -10.953 19.594 1.00 42.54	PROT
45	ATOM	305 CE2 PHE 245	53.652 -8.989 19.936 1.00 45.84	PROT
	ATOM	306 CZ PHE 245	52.835 -9.988 20.443 1.00 33.72	PROT
	ATOM	307 C PHE 245	53.549 -8.693 14.068 1.00 38.75	PROT
	ATOM	308 O PHE 245	53.794 -9.660 13.337 1.00 48.93	PROT
	ATOM	309 N LEU 246	53.789 -7.437 13.704 1.00 41.18	PROT
50	ATOM	310 CA LEU 246	54.362 -7.124 12.404 1.00 43.43	PROT

	ATOM	311 CB LEU 246 54	4.378 -5.612 12.181 1.00 42.78	PROT
	ATOM		4.535 -5.200 10.718 1.00 49.88	PROT
	ATOM	313 CD1 LEU 246 5	3.528 -4.113 10.365 1.00 40.64	PROT
	ATOM	314 CD2 LEU 246 5	5.966 -4.730 10.485 1.00 48.66	PROT
5	ATOM	315 C LEU 246 55	.777 -7.692 12.250 1.00 42.60	PROT
	ATOM	316 O LEU 246 56	.677 -7.383 13.028 1.00 45.75	PROT
	ATOM	317 N PRO 247 55	.977 -8.540 11.233 1.00 50.03	PROT
	ATOM	318 CD PRO 247 5	4.914 -8.924 10.286 1.00 60.17	PROT
	ATOM		7.237 -9.199 10.894 1.00 49.90	PROT
10	ATOM		7.181 -9.282 9.369 1.00 59.51	PROT
	ATOM		5.678 -9.244 9.023 1.00 52.86	PROT
	ATOM		.499 -8.494 11.392 1.00 48.85	PROT
	ATOM		.675 -7.295 11.186 1.00 49.28	PROT
	ATOM		0.379 -9.261 12.032 1.00 47.62	PROT
15	ATOM		0.628 -8.733 12.574 1.00 51.41	PROT
•	ATOM		1.266 -9.750 13.522 1.00 44.22	PROT
	ATOM		.623 -8.354 11.490 1.00 53.28	PROT
	ATOM		.815 -8.214 11.765 1.00 62.57	PROT
•	ATOM		.146 -8.200 10.258 1.00 56.20	PROT
20	ATOM		2.030 -7.818 9.164 1.00 55.88	PROT
	ATOM		2.231 -8.981 8.173 1.00 53.88	PROT
	ATOM		0.928 -9.637 7.739 1.00 54.39	
	ATOM		0.578 -10.693 8.310 1.00 57.70	
	ATOM		60.264 -9.112 6.819 1.00 45.76	PROT
25	ATOM		.539 -6.567 8.437 1.00 54.20	PROT
	ATOM		.119 -6.154 7.429 1.00 55.31	PROT
	ATOM		469 -5.965 8.954 1.00 46.13	PROT
	ATOM		.933 -4.735 8.376 1.00 46.12	PROT
20	ATOM		.413 -4.764 8.253 1.00 43.38	PROT
30	ATOM		7.892 -3.344 8.057 1.00 39.15	PROT
	ATOM		8.007 -5.654 7.074 1.00 48.96	PROT PROT
	ATOM		5.707 -6.401 7.283 1.00 43.14 311 -3.590 9.294 1.00 45.32	PROT
	ATOM		257 -3.724 10.513 1.00 43.74	PROT
25	ATOM		0.680 -2.459 8.711 1.00 36.80	PROT
35	ATOM ATOM		51.091 -1.329 9.521 1.00 39.28	PROT
	ATOM		1.370 -1.621 10.305 1.00 44.31	PROT
	ATOM		2.538 -1.145 11.428 1.00 51.39	PROT
	ATOM		3.277 -2.399 9.715 1.00 55.47	PROT
40	ATOM		4.536 -2.745 10.374 1.00 54.24	PROT
40	ATOM		4.792 -4.237 10.245 1.00 49.31	PROT
	ATOM		5.720 -1.959 9.812 1.00 54.86	PROT
	ATOM		5.492 -1.079 8.953 1.00 58.80	PROT
	ATOM		0.887 6.759 5.510 1.00 34.33	PROT
45	ATOM		59.550 6.086 5.790 1.00 34.34	PROT
43	ATOM		60.893 8.163 6.080 1.00 20.22	PROT
	ATOM		2.053 4.557 5.439 1.00 34.08	PROT
	ATOM		2.280 4.466 4.232 1.00 46.39	PROT
	ATOM		3.361 6.605 5.966 1.00 21.27	PROT
50	ATOM		52.041 5.920 6.122 1.00 29.68	PROT

	ATOM	361 N ASP 265	61.809 3.499 6.209 1.00 40.63	PROT
	ATOM	362 CA ASP 265	61.796 2.141 5.670 1.00 43.58	PROT
	ATOM	363 CB ASP 265	61.243 1.160 6.704 1.00 44.07	PROT
	ATOM	364 CG ASP 265	61.179 -0.262 6.185 1.00 49.19	PROT
5	ATOM	365 OD1 ASP 265	62.223 -0.945 6.175 1.00 57.67	PROT
	ATOM	366 OD2 ASP 265	60.082 -0.702 5.789 1.00 54.75	PROT
	ATOM	367 C ASP 265	60.956 2.071 4.401 1.00 48.03	PROT
	ATOM	368 O ASP 265	61.362 1.458 3.411 1.00 57.44	PROT
	ATOM	369 N LEU 266	59.793 2.711 4.436 1.00 40.55	PROT
10	ATOM	370 CA LEU 266	58.879 2.741 3.295 1.00 45.78	PROT
_	ATOM	371 CB LEU 266	59.638 2.962 1.977 1.00 45.92	PROT
	ATOM	372 CG LEU 266	59.881 4.407 1.506 1.00 48.41	PROT
	ATOM	373 CD1 LEU 266	59.934 4.432 -0.007 1.00 32.83	PROT
	ATOM	374 CD2 LEU 266	58.787 5.344 2.012 1.00 45.08	PROT
15	ATOM	375 C LEU 266	58.064 1.462 3.214 1.00 45.45	PROT
	ATOM	376 O LEU 266	56.862 1.503 2.949 1.00 42.92	PROT
	ATOM	377 N GLU 267	58.712 0.324 3.431 1.00 46.47	PROT
	ATOM	378 CA GLU 267	57.986 -0.935 3.415 1.00 44.34	PROT
	ATOM	379 CB GLU 267	58.943 -2.123 3.505 1.00 39.42	PROT
20	ATOM	380 CG GLU 267	58.291 -3.457 3.188 1.00 40.68	PROT
	ATOM	381 CD GLU 267	58.929 -4.607 3.943 1.00 63.54	PROT
	ATOM	382 OE1 GLU 267	60.103 -4.470 4.361 1.00 68.92	PROT
	ATOM	383 OE2 GLU 267	58.258 -5.650 4.120 1.00 66.66	PROT
	ATOM	384 C GLU 267	57.106 -0.880 4.655 1.00 41.57	PROT
25	ATOM	385 O GLU 267	55.991 -1.398 4.673 1.00 48.68	PROT
	ATOM	386 N ALA 268	57.620 -0.215 5.686 1.00 39.33	PROT
	ATOM	387 CA ALA 268	56.916 -0.057 6.951 1.00 31.62	PROT
	ATOM	388 CB ALA 268	57.918 0.134 8.063 1.00 7.56	PROT
	ATOM	389 C ALA 268	55.960 1.135 6.888 1.00 25.96	PROT
30	ATOM	390 O ALA 268	54.786 1.036 7.237 1.00 17.35	PROT
	ATOM	391 N PHE 269	56.464 2.274 6.446 1.00 11.34	PROT
	ATOM	392 CA PHE 269	55.615 3.453 6.335 1.00 15.72	PROT
	ATOM	393 CB PHE 269	56.274 4.474 5.405 1.00 20.08	PROT
	ATOM	394 CG PHE 269	55.552 5.788 5.334 1.00 24.67	PROT
35	ATOM	395 CD1 PHE 269	55.661 6.713 6.369 1.00 15.69	PROT
	ATOM	396 CD2 PHE 269	54.772 6.111 4.222 1.00 20.64	PROT
	ATOM	397 CE1 PHE 269	55.003 7.942 6.300 1.00 22.55	PROT
	ATOM	398 CE2 PHE 269	54.108 7.342 4.143 1.00 19.77	PROT
	ATOM	399 CZ PHE 269	54.224 8.257 5.186 1.00 19.27	PROT
40	ATOM	400 C PHE 269	54.277 3.010 5.754 1.00 19.45	PROT
	ATOM	401 O PHE 269	53.212 3.351 6.261 1.00 13.40	PROT
	ATOM	402 N SER 270	54.367 2.214 4.692 1.00 43.85	PROT
	ATOM	403 CA SER 270	53.217 1.686 3.967 1.00 46.67	PROT
	ATOM	404 CB SER 270	53.687 0.669 2.924 1.00 53.60	PROT
45	ATOM	405 OG SER 270	52.662 0.382 1.988 1.00 68.82	PROT
	ATOM	406 C SER 270	52.181 1.039 4.865 1.00 43.32	PROT
	ATOM	407 O SER 270	51.024 1.459 4.893 1.00 43.87	PROT
	ATOM	408 N HIS 271	52.594 0.009 5.590 1.00 34.59	PROT
	ATOM	409 CA HIS 271	51.681 -0.694 6.486 1.00 37.12	PROT
50	ATOM	410 CB HIS 271	52.441 -1.772 7.266 1.00 46.61	PROT

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PROT
    ATOM 411 CG HIS 271
                              52.603 -3.056 6.512 1.00 63.99
                              51.879 -4.201 6.533 1.00 62.06
                                                           PROT
           412 CD2 HIS 271
    ATOM
                              53.608 -3.256 5.590 1.00 60.86
                                                           PROT
    ATOM 413 ND1 HIS 271
                              53.497 -4.467 5.075 1.00 60.70
    ATOM 414 CE1 HIS 271
                                                           PROT
                              52.456 -5.061 5.630 1.00 64.10
                                                           PROT
           415 NE2 HIS 271
    ATOM
    ATOM 416 C HIS 271
                             50.973 0.261 7.459 1.00 36.53
                                                          PROT
                             49.744 0.245 7.586 1.00 37.75
                                                          PROT
    ATOM 417 O HIS 271
                                                          PROT
                             51.752 1.099 8.133 1.00 32.81
    ATOM 418 N PHE 272
                              51.190 2.038 9.085 1.00 27.77
                                                           PROT
    ATOM 419 CA PHE 272
                              52.302 2.886 9.714 1.00 10.49
                                                           PROT
10
    ATOM 420 CB PHE 272
                              53.338 2.086 10.459 1.00 6.98
    ATOM 421 CG PHE 272
                                                           PROT
                               54.671 2.478 10.449 1.00 4.13
                                                           PROT
    ATOM 422 CD1 PHE 272
                               52.978 0.961 11.193 1.00 6.95
                                                           PROT
    ATOM 423 CD2 PHE 272
    ATOM 424 CE1 PHE 272
                               55.634 1.764 11.163 1.00 7.86
                                                           PROT
    ATOM 425 CE2 PHE 272
                              53.930 0.242 11.909 1.00 6.13
                                                           PROT
15
                              55.263 0.645 11.895 1.00 8.93
                                                           PROT
    ATOM 426 CZ PHE 272
                             50.168 2.939 8.405 1.00 30.96
                                                          PROT
    ATOM 427 C PHE 272
                             49.071 3.156 8.931 1.00 30.21
                                                          PROT
    ATOM 428 O PHE 272
    ATOM 429 N THR 273
                              50.522 3.452 7.231 1.00 31.55
                                                          PROT
    ATOM 430 CA THR 273
                              49.633 4.343 6.487 1.00 33.39
                                                           PROT
20
    ATOM 431 CB THR 273
                              50.335 4.912 5.243 1.00 36.80
                                                           PROT
                               50.649 3.847 4.332 1.00 27.42
    ATOM 432 OG1 THR 273
                                                            PROT
                               51.613 5.641 5.656 1.00 32.25
                                                            PROT
    ATOM 433 CG2 THR 273
                             48.350 3.647 6.056 1.00 34.07
    ATOM 434 C THR 273
                                                          PROT
                              47.362 4.294 5.697 1.00 17.11
    ATOM 435 O THR 273
                                                           PROT
25
                             48.372 2.321 6.088 1.00 34.47
                                                          PROT
    ATOM 436 N LYS 274
                              47.196 1.555 5.726 1.00 42.17
                                                           PROT
    ATOM 437 CA LYS 274
                              47.544 0.069 5.615 1.00 40.02
                                                           PROT
    ATOM 438 CB LYS 274
                             46.153 1.778 6.818 1.00 41.47
    ATOM 439 C LYS 274
                                                          PROT
                             45.115 2.402 6.584 1.00 47.37
                                                          PROT
    ATOM 440 O LYS 274
30
                             46.456 1.290 8.019 1.00 34.08
                                                          PROT
    ATOM 441 N ILE 275
    ATOM 442 CA ILE 275
                              45.559 1.403 9.166 1.00 25.49
                                                          PROT
                             45.991 0.435 10.262 1.00 19.72
                                                           PROT
    ATOM
           443 CB ILE 275
                              46.290 -0.934 9.642 1.00 23.39
                                                           PROT
    ATOM
           444 CG2 ILE 275
           445 CG1 ILE 275
                              47.249 0.958 10.953 1.00 12.96
                                                           PROT
    ATOM
35
                              47.970 -0.103 11.769 1.00 11.07
    ATOM 446 CD1 ILE 275
                                                           PROT
                             45.440 2.805 9.762 1.00 20.03
                                                         PROT
    ATOM 447 C ILE 275
    ATOM 448 O ILE 275
                             44.541 3.081 10.547 1.00 18.98
                                                          PROT
                             46.347 3.694 9.402 1.00 8.88
    ATOM 449 N ILE 276
                                                         PROT
                              46.268 5.043 9.924 1.00 6.62
                                                          PROT
           450 CA ILE 276
40
    ATOM
                                                          PROT
    ATOM 451 CB ILE 276
                              47.298 5.972 9.261 1.00 21.77
                              46.894 6.267 7.831 1.00 27.28
    ATOM 452 CG2 ILE 276
                                                           PROT
                              47.374 7.288 10.028 1.00 6.75
                                                           PROT
           453 CG1 ILE 276
    ATOM
    ATOM 454 CD1 ILE 276
                              48.349 7.255 11.153 1.00 15.44
                                                           PROT
                             44.887 5.649 9.697 1.00 12.17
                                                          PROT
           455 C ILE 276
45
    ATOM
           456 O ILE 276
                             44.349 6.331 10.565 1.00 29.36
                                                          PROT
    ATOM
                              44.303 5.411 8.535 1.00 22.12
                                                           PROT
    ATOM 457 N THR 277
                              43.007 6.005 8.260 1.00 27.16
                                                           PROT
    ATOM 458 CA THR 277
                              42.532 5.675 6.834 1.00 27.11
    ATOM 459 CB THR 277
                                                           PROT
                              43.665 5.584 5.955 1.00 22.55
                                                           PROT
50
    ATOM 460 OG1 THR 277
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	A TO \ 4	ACL CC2 TUD 277 ALSOA C 7C2 C 227 1 00 2C 00	PROT
	ATOM		PROT
	ATOM		PROT
	ATOM		PROT
-	ATOM		PROT
5	ATOM	2	PROT
	ATOM		
	ATOM	467 CB PRO 278 40.907 2.280 10.415 1.00 14.77	PROT
	ATOM	468 CG PRO 278 42.195 2.008 9.738 1.00 7.70	PROT
	ATOM	469 C PRO 278 40.956 4.356 11.870 1.00 25.40	PROT
10	ATOM	470 O PRO 278 39.983 4.628 12.576 1.00 22.33	PROT
	ATOM	471 N ALA 279 42.211 4.507 12.285 1.00 22.14	PROT
	ATOM	472 CA ALA 279 42.519 5.038 13.607 1.00 20.26	PROT
	ATOM	473 CB ALA 279 44.016 5.033 13.831 1.00 13.33	PROT
	ATOM	474 C ALA 279 41.984 6.456 13.699 1.00 16.49	PROT
15	ATOM	475 O ALA 279 41.222 6.797 14.598 1.00 32.38	PROT
	ATOM		ROT
	ATOM	, , , , ,	PROT
	ATOM		PROT
	ATOM	479 CG2 ILE 280 42.172 10.871 11.581 1.00 2.00	PROT
20	ATOM	480 CG1 ILE 280 43.901 9.059 11.220 1.00 10.96	PROT
	ATOM	481 CD1 ILE 280 44.615 10.036 10.294 1.00 8.54	PROT
	ATOM		PROT
	ATOM		PROT
	ATOM	484 N THR 281 39.692 7.883 12.172 1.00 24.18	PROT
25	ATOM	485 CA THR 281 38.238 7.962 12.153 1.00 24.77	PROT
	ATOM	486 CB THR 281 37.650 6.952 11.145 1.00 33.90	PROT
	ATOM	487 OG1 THR 281 38.607 6.711 10.108 1.00 34.62	PROT
	ATOM	488 CG2 THR 281 36.379 7.506 10.513 1.00 39.80	PROT
	ATOM	489 C THR 281 37.655 7.726 13.535 1.00 23.39	PROT
30	ATOM	490 O THR 281 36.733 8.422 13.960 1.00 19.51	PROT
	ATOM	491 N ARG 282 38.213 6.743 14.234 1.00 16.90	PROT
	ATOM	492 CA ARG 282 37.781 6.404 15.583 1.00 12.29	PROT
	ATOM	493 CB ARG 282 38.641 5.260 16.115 1.00 5.36	PROT
	ATOM	494 CG ARG 282 37.936 3.926 16.136 1.00 17.05	PROT
35	ATOM	495 CD ARG 282 38.296 3.095 14.942 1.00 18.41	PROT
	ATOM	496 NE ARG 282 39.622 2.475 15.011 1.00 35.77	PROT
	ATOM	497 CZ ARG 282 40.454 2.501 16.055 1.00 36.80	PROT
	ATOM	498 NH1 ARG 282 41.629 1.888 15.967 1.00 35.96	PROT
	ATOM	499 NH2 ARG 282 40.134 3.120 17.183 1.00 25.20	PROT
40	ATOM	500 C ARG 282 37.863 7.626 16.520 1.00 16.75	PROT
	ATOM	501 O ARG 282 37.078 7.758 17.456 1.00 22.98	PROT
	ATOM	502 N VAL 283 38.813 8.518 16.268 1.00 11.92	PROT
	ATOM	503 CA VAL 283 38.937 9.719 17.083 1.00 14.68	PROT
	ATOM	504 CB VAL 283 . 40.191 10.541 16.696 1.00 23.35	PROT
45	ATOM	505 CG1 VAL 283 40.467 11.593 17.752 1.00 11.98	PROT
	ATOM	506 CG2 VAL 283 41.396 9.621 16.526 1.00 20.41	PROT
	ATOM	507 C VAL 283 37.705 10.580 16.833 1.00 12.72	PROT
	ATOM	508 O VAL 283 36.965 10.929 17.752 1.00 20.37	PROT
	ATOM	509 N VAL 284 37.503 10.920 15.567 1.00 18.28	PROT
50	ATOM	510 CA VAL 284 36.369 11.727 15.150 1.00 16.98	PROT

	•			
	ATOM	511 CB VAL 284.		PROT
	ATOM	512 CG1 VAL 284	35.434 12.973 13.172 1.00 19.30	
	ATOM	513 CG2 VAL 284	37.649 11.794 12.959 1.00 16.94	
	ATOM	514 C VAL 284	35.113 11.093 15.715 1.00 14.89	PROT
5	ATOM	515 O VAL 284	34.233 11.781 16.219 1.00 10.93	PROT
	ATOM	516 N ASP 285	35.046 9.768 15.623 1.00 10.68	PROT
	ATOM	517 CA ASP 285	33.898 9.022 16.114 1.00 20.76	PROT
	ATOM	518 CB ASP 285	34.079 7.518 15.874 1.00 22.99	PROT
	ATOM	519 CG ASP 285	33.985 7.130 14.397 1.00 30.01	PROT
10	ATOM	520 OD1 ASP 285	33.185 7.735 13.648 1.00 18.56	PROT
	ATOM	521 OD2 ASP 285	34.720 6.202 13.993 1.00 27.74	PROT
	ATOM	522 C ASP 285	33.734 9.274 17.604 1.00 26.87	PROT
	ATOM	523 O ASP 285	32.609 9.349 18.103 1.00 39.89	PROT
	ATOM	524 N PHE 286	34.861 9.405 18.308 1.00 25.45	PROT
15	ATOM	525 CA PHE 286	34.862 9.654 19.746 1.00 15.66	PROT
	ATOM	526 CB PHE 286	36.284 9.533 20.305 1.00 7.30	PROT
	ATOM	527 CG PHE 286	36.454 10.104 21.703 1.00 17.92	PROT
	ATOM	528 CD1 PHE 286	35.848 9.499 22.805 1.00 19.35	PROT
	ATOM	529 CD2 PHE 286	37.229 11.245 21.920 1.00 19.24	PROT
20	ATOM	530 CE1 PHE 286	36.014 10.021 24.087 1.00 9.94	PROT
	ATOM	531 CE2 PHE 286	37.395 11.769 23.207 1.00 11.33	
	ATOM	532 CZ PHE 286	36.786 11.154 24.283 1.00 2.00	PROT
	ATOM	533 C PHE 286	34.313 11.043 20.030 1.00 17.67	PROT
	ATOM	534 O PHE 286	33.367 11.201 20.797 1.00 14.36	PROT
25	ATOM	535 N ALA 287	34.905 12.056 19.410 1.00 12.57	PROT
	ATOM	536 CA ALA 287	34.443 13.426 19.622 1.00 12.49	PROT
	ATOM	537 CB ALA 287	35.250 14.386 18.759 1.00 23.54	PROT
	ATOM	538 C ALA 287	32.954 13.559 19.307 1.00 9.21	PROT
	ATOM	539 O ALA 287	32.209 14.205 20.043 1.00 11.68	PROT
30	ATOM	540 N LYS 288	32.540 12.929 18.209 1.00 16.43	PROT
	ATOM	541 CA LYS 288	31.157 12.944 17.736 1.00 16.10	PROT
	ATOM	542 CB LYS 288	31.003 11.977 16.569 1.00 13.15	PROT
	ATOM	543 CG LYS 288	31.117 12.636 15.219 1.00 25.55	PROT
	ATOM	544 CD LYS 288	30.480 11.779 14.136 1.00 32.95	PROT
35	ATOM	545 CE LYS 288	31.279 10.507 13.900 1.00 34.58	PROT
	ATOM	546 NZ LYS 288	30.755 9.721 12.748 1.00 36.93	PROT
	ATOM	547 C LYS 288	30.154 12.569 18.813 1.00 18.87	PROT
	ATOM	548 O LYS 288	29.078 13.171 18.917 1.00 12.83	PROT
	ATOM	549 N LYS 289	30.525 11.574 19.614 1.00 11.81	PROT
40	ATOM	.550 CA LYS 289	29.674 11.067 20.681 1.00 15.53	PROT
	ATOM	551 CB LYS 289	30.070 9.631 21.011 1.00 15.88	PROT
	ATOM	552 CG LYS 289	29.767 8.645 19.911 1.00 20.93	PROT
	ATOM	553 CD LYS 289	29.140 7.382 20.471 1.00 28.97	PROT
	ATOM	554 CE LYS 289	29.951 6.167 20.071 1.00 25.06	PROT
45	ATOM	555 NZ LYS 289	30.043 6.060 18.590 1.00 39.19	PROT
	ATOM	556 C LYS 289	29.660 11.884 21.969 1.00 15.95	PROT
	ATOM	557 O LYS 289	29.205 11.398 23.001 1.00 28.53	PROT
	ATOM	558 N LEU 290	30.151 13.116 21.919 1.00 10.13	PROT
	ATOM	559 CA LEU 290	30.155 13.959 23.104 1.00 7.83	PROT
50	ATOM	560 CB LEU 290	31.588 14.300 23.532 1.00 14.46	PROT

	ATOM	561 CG LEU 290	32.676 13.228 23.542 1.00 11.22 34.016 13.900 23.678 1.00 3.02	PROT PROT
	ATOM	562 CD1 LEU 290	32.449 12.257 24.686 1.00 9.39	PROT
	ATOM	563 CD2 LEU 290 564 C LEU 290	29.410 15.259 22.849 1.00 7.59	PROT
5	ATOM	564 C LEU 290 565 O LEU 290	29.942 16.148 22.196 1.00 11.01	PROT
5	ATOM ATOM	566 N PRO 291	28.169 15.381 23.365 1.00 14.33	PROT
	ATOM	567 CD PRO 291	27.515 14.291 24.109 1.00 18.52	PROT
	ATOM	568 CA PRO 291	27.290 16.556 23.240 1.00 6.61	PROT
	ATOM	569 CB PRO 291	26.296 16.400 24.384 1.00 11.95	PROT
10	ATOM	570 CG PRO 291	26.496 15.004 24.929 1.00 20.22	PROT
10	ATOM	571 C PRO 291	28.029 17.885 23.332 1.00 14.74	PROT
	ATOM	572 O PRO 291	27.795 18.792 22.537 1.00 26.09	PROT
	ATOM	573 N MET 292	28.917 18.002 24.315 1.00 24.06	PROT
	ATOM	574 CA MET 292	29.697 19.225 24.494 1.00 25.33	PROT
15	ATOM	575 CB MET 292	30.706 19.046 25.628 1.00 26.65	PROT
13	ATOM	576 CG MET 292	30.222 19.581 26.962 1.00 26.97	PROT
	ATOM	577 SD MET 292	31.153 18.943 28.362 1.00 29.01	PROT
	ATOM	578 CE MET 292	30.315 17.438 28.685 1.00 17.91	PROT
	ATOM	579 C MET 292	30.430 19.588 23.204 1.00 23.01	PROT
20	ATOM	580 O MET 292	30.478 20.747 22.813 1.00 31.98	PROT
20	ATOM	581 N PHE 293	31.007 18.591 22.547 1.00 23.44	PROT
	ATOM	582 CA PHE 293	31.724 18.819 21.297 1.00 24.83	PROT
	ATOM	583 CB PHE 293	32.389 17.529 20.830 1.00 15.05	PROT
	ATOM	584 CG PHE 293	33.214 17.686 19.594 1.00 13.55	PROT
25	ATOM	585 CD1 PHE 293	34.376 18.446 19.614 1.00 19.86	PROT
	ATOM	586 CD2 PHE 293	32.867 17.024 18.425 1.00 22.99	PROT
	ATOM	587 CE1 PHE 293	35.184 18.540 18.495 1.00 18.15	PROT
	ATOM	588 CE2 PHE 293	33.671 17.108 17.291 1.00 20.83	PROT
	ATOM	589 CZ PHE 293	34.831 17.866 17.328 1.00 22.53	PROT
30	ATOM	590 C PHE 293	30.759 19.291 20.222 1.00 27.26	PROT
	ATOM	591 O PHE 293	30.971 20.319 19.577 1.00 28.69	PROT
	ATOM	592 N CYS 294	29.689 18.528 20.040 1.00 29.92	PROT
	ATOM	593 CA CYS 294	28.700 18.855 19.037 1.00 35.54	PROT
	ATOM	594 CB CYS 294	27.540 17.860 19.106 1.00 19.11	PROT
35	ATOM	595 SG CYS 294	27.843 16.358 18.132 1.00 35.66	PROT
	ATOM	596 C CYS 294	28.203 20.291 19.171 1.00 38.84	PROT
	ATOM	597 O CYS 294	28.072 20.995 18.169 1.00 45.94	PROT
	ATOM	598 N GLU 295	27.959 20.739 20.401 1.00 27.34	PROT
	ATOM	599 CA GLU 295	27.472 22.097 20.632 1.00 21.06	PROT
40	ATOM	600 CB GLU 295	27.178 22.306 22.121 1.00 29.78	PROT
	ATOM	601 C GLU 295	28.458 23.158 20.128 1.00 23.67	PROT
	ATOM	602 O GLU 295	28.228 24.357 20.272 1.00 29.89	PROT
	ATOM	603 N LEU 296	29.551 22.715 19.522 1.00 21.46	PROT
	ATOM	604 CA LEU 296	30.545 23.642 19.005 1.00 26.35	PROT
45	ATOM	605 CB LEU 296	31.947 23.128 19.330 1.00 25.17	PROT
	ATOM	606 CG LEU 296	32.419 23.157 20.778 1.00 13.78	PROT
	ATOM	607 CD1 LEU 296	33.593 22.217 20.931 1.00 23.61	PROT
	ATOM	608 CD2 LEU 296	32.814 24.564 21.160 1.00 13.82	PROT
	ATOM	609 C LEU 296	30.415 23.783 17.493 1.00 31.88	PROT
50	ATOM	610 O LEU 296	29.890 22.890 16.827 1.00 45.99	PROT

	ATOM	611 N PRO 297	30.884 24.912 16.932 1.00 27.00	PROT
	ATOM	612 CD PRO 297	31.423 26.037 17.708 1.00 36.12	PROT
	ATOM	613 CA PRO 297	30.856 25.222 15.492 1.00 22.30	PROT
	ATOM	614 CB PRO 297	31.182 26.716 15.424 1.00 16.06	PROT
5	ATOM	615 CG PRO 297	31.107 27.208 16.827 1.00 42.41	PROT
-	ATOM	616 C PRO 297	31.838 24.413 14.642 1.00 28.19	PROT
	ATOM	617 O PRO 297	32.983 24.189 15.036 1.00 39.38	PROT
	ATOM	618 N CYS 298	31.371 24.014 13.457 1.00 35.37	PROT
	ATOM	619 CA CYS 298	32.134 23.233 12.481 1.00 32.41	PROT
10	ATOM	620 CB CYS 298	31.416 23.289 11.112 1.00 40.85	PROT
10	ATOM	621 SG CYS 298	32.431 23.615 9.614 1.00 61.24	PROT
	ATOM	622 C CYS 298	33.596 23.654 12.352 1.00 31.68	PROT
	ATOM	623 O CYS 298	34.474 22.804 12.225 1.00 28.49	PROT
	ATOM	624 N GLU 299	33.869 24.954 12.393 1.00 29.93	PROT
15	ATOM	625 CA GLU 299	35.253 25.407 12.278 1.00 36.38	PROT
13	ATOM	626 CB GLU 299	35.346 26.931 12.203 1.00 32.78	PROT
	ATOM	627 CG GLU 299	34.467 27.546 11.167 1.00 43.40	PROT
	ATOM	628 CD GLU 299	33.038 27.593 11.625 1.00 58.19	PROT
	ATOM	629 OE1 GLU 299	32.723 28.457 12.474 1.00 67.37	PROT
20	ATOM	630 OE2 GLU 299	32.237 26.762 11.143 1.00 54.02	PROT
20	ATOM	631 C GLU 299	36.057 24.932 13.475 1.00 38.89	PROT
	ATOM	632 O GLU 299	37.129 24.342 13.316 1.00 48.67	PROT
	ATOM	633 N ASP 300	35.528 25.186 14.671 1.00 36.49	PROT
	ATOM	634 CA ASP 300	36.201 24.805 15.906 1.00 29.96	PROT
25	ATOM	635 CB ASP 300	35.455 25.391 17.111 1.00 5.33	PROT
2,5	ATOM	636 CG ASP 300	35.830 26.853 17.378 1.00 19.10	PROT
	ATOM	637 OD1 ASP 300	36.491 27.473 16.518 1.00 27.28	PROT
	ATOM	638 OD2 ASP 300	35.470 27.396 18.444 1.00 23.55	PROT
	ATOM	639 C ASP 300	36.380 23.294 16.054 1.00 25.88	PROT
30	ATOM	640 O ASP 300	37.441 22.845 16.484 1.00 19.03	PROT
50	ATOM	641 N GLN 301	35.360 22.516 15.689 1.00 6.29	PROT
	ATOM	642 CA GLN 301	35.432 21.055 15.769 1.00 9.51	PROT
	ATOM	643 CB GLN 301	34.170 20.421 15.183 1.00 18.27	PROT
	ATOM	644 CG GLN 301	32.886 20.813 15.875 1.00 28.72	PROT
35	ATOM	645 CD GLN 301	31.676 20.155 15.243 1.00 17.63	PROT
•	ATOM	646 OE1 GLN 301	31.689 19.823 14.060 1.00 30.65	PROT
	ATOM	647 NE2 GLN 301	30.625 19.965 16.027 1.00 30.44	PROT
	ATOM	648 C GLN 301	36.646 20.491 15.020 1.00 15.48	PROT
	ATOM	649 O GLN 301	37.333 19.584 15.500 1.00 21.96	PROT
40	ATOM		36.891 21.014 13.825 1.00 24.00	PROT
	ATOM	651 CA ILE 302	38.011 20.555 13.026 1.00 28.84	PROT
	ATOM	652 CB ILE 302	37.930 21.112 11.607 1.00 33.13	PROT
	ATOM	653 CG2 ILE 302	39.147 20.690 10.813 1.00 37.90	PROT
	ATOM	654 CG1 ILE 302	36.656 20.610 10.941 1.00 29.63	PROT
45	ATOM	655 CD1 ILE 302	36.296 21.356 9.698 1.00 32.99	PROT
13	ATOM		39.308 21.014 13.670 1.00 28.73	PROT
	ATOM		40.219 20.219 13.895 1.00 36.02	PROT
	ATOM		39.396 22.304 13.968 1.00 25.04	PROT
	ATOM	659 CA ILE 303	40.590 22.817 14.603 1.00 24.27	PROT
50	ATOM	660 CB ILE 303	40.414 24.270 15.054 1.00 20.89	PROT
50	7110111	OUR CIT IND DOD		

	ATOM		1.686 24.740 15.744 1.00 32.38	PROT
	ATOM		0.079 25.158 13.849 1.00 18.88	PROT
	ATOM	_	0.298 26.648 14.079 1.00 5.31	PROT
	ATOM		861 21.948 15.825 1.00 26.92	PROT
5	ATOM		963 21.440 15.997 1.00 31.32	PROT
	ATOM		2.843 21.763 16.659 1.00 11.00	PROT
	ATOM	· · · · · · · · · · · · · · · · · · ·	9.983 20.953 17.854 1.00 7.21	PROT
	ATOM		8.663 20.886 18.613 1.00 2.00	PROT
	ATOM		8.633 21.511 20.012 1.00 8.04	PROT
10	ATOM		39.383 22.812 19.997 1.00 2.00	PROT
	ATOM		37.188 21.729 20.472 1.00 4.99	PROT
	ATOM		.441 19.554 17.507 1.00 4.64	PROT
	ATOM		.368 19.032 18.119 1.00 14.88	PROT
	ATOM		0.807 18.953 16.510 1.00 4.55	PROT
15	ATOM		0.140 17.590 16.093 1.00 7.03	PROT
	ATOM	· · · · · · · · · · · · · · · · · · ·	9.099 17.098 15.104 1.00 3.70	PROT
	ATOM		8.164 16.054 15.691 1.00 10.31	PROT
	ATOM	•	36.744 16.340 15.245 1.00 2.00	PROT
	ATOM	*·•	38.629 14.665 15.260 1.00 9.42	PROT
20	ATOM		.527 17.418 15.483 1.00 10.17	PROT
	ATOM		2.174 16.374 15.651 1.00 7.58	PROT
	ATOM		.975 18.442 14.765 1.00 9.98	PROT
	ATOM		3.283 18.408 14.127 1.00 9.14	PROT
	ATOM		3.409 19.558 13.131 1.00 18.85	PROT
25	ATOM		2.815 19.270 11.763 1.00 25.44	PROT
	ATOM		2.198 20.529 11.178 1.00 29.07	PROT
	ATOM	· · · · · · · · · · · · · · · · · · ·	2.698 20.808 9.774 1.00 37.81	PROT
	ATOM		3.867 19.964 9.403 1.00 30.48	PROT
	ATOM		.376 18.522 15.175 1.00 7.31	PROT
30	ATOM		.439 17.919 15.048 1.00 16.95	PROT
	ATOM		1.097 19.295 16.218 1.00 12.67	PROT
	ATOM		15.062 19.484 17.279 1.00 7.25	PROT
	ATOM		5.297 18.269 18.150 1.00 15.08	PROT
	ATOM		5.441 17.972 18.488 1.00 20.11	PROT
35	ATOM		1.225 17.552 18.481 1.00 8.29	PROT
	ATOM		4.286 16.380 19.364 1.00 3.44	PROT
	ATOM		3.097 16.402 20.326 1.00 14.26	PROT
	ATOM		1.539 15.750 19.634 1.00 21.83	PROT
	ATOM		1.344 14.995 18.738 1.00 8.37	PROT
40	ATOM		1.502 13.997 19.453 1.00 10.98	PROT
	ATOM		1.202 14.916 17.420 1.00 10.83	PROT
	ATOM		4.236 13.625 16.752 1.00 3.22	PROT
	ATOM		4.240 13.831 15.240 1.00 15.79	PROT
	ATOM		3.683 12.402 14.319 1.00 25.54	PROT
45	ATOM		5.439 12.767 17.193 1.00 2.00	PROT
	ATOM		5.251 11.722 17.807 1.00 12.28	PROT
	ATOM		6.663 13.205 16.900 1.00 2.00	PROT
	ATOM		47.858 12.446 17.286 1.00 2.00	PROT
	ATOM	709 CB MET 310	49.122 13.171 16.860 1.00 2.00	PROT
50	ATOM	710 CG MET 310	49.975 12.422 15.880 1.00 5.92	PROT

		511 CD MET 310 60	401 10 005 16 769 1 00 22 47	ррот
	ATOM		481 10.805 16.368 1.00 22.47	
	ATOM		140 11.112 16.808 1.00 20.84	PROT PROT
	ATOM		941 12.239 18.793 1.00 11.95	
_	ATOM		455 11.220 19.270 1.00 15.53	PROT
5	ATOM		163 13.225 19.542 1.00 6.79	PROT
	ATOM		.493 13.139 20.979 1.00 2.00	PROT
	ATOM		932 14.427 21.581 1.00 6.42	PROT
	ATOM		.880 15.619 21.436 1.00 8.40	
	ATOM		236 16.940 21.820 1.00 14.10	
10	ATOM		1.157 16.895 22.434 1.00 16.54	
	ATOM		7.795 18.020 21.515 1.00 4.09	
	ATOM		583 11.923 21.406 1.00 7.80	PROT
	ATOM		95 11.026 22.067 1.00 14.07	PROT
	ATOM		25 11.873 21.001 1.00 2.00	PROT
15	ATOM		574 10.752 21.371 1.00 3.60	PROT
	ATOM		14 11.013 20.947 1.00 2.00	PROT
	ATOM		277 9.769 21.145 1.00 2.00	PROT
	ATOM		579 12.221 21.727 1.00 2.00	PROT
	ATOM		118 12.555 21.495 1.00 2.00	PROT
20	ATOM		9 9.437 20.760 1.00 8.32	PROT
	ATOM	731 O ILE 312 44.91		PROT
	ATOM		515 9.501 19.563 1.00 3.98	PROT
	ATOM	-	.054 8.282 18.905 1.00 8.91	PROT
~ ~	ATOM		.455 8.572 17.462. 1.00 25.71	PROT
25	ATOM		.430 8.111 16.431 1.00 22.86	
	ATOM		955 8.430 14.736 1.00 20.60	PROT
	ATOM		.412 10.055 14.534 1.00 14.95	
	ATOM	738 C MET 313 47.2		PROT PROT
30	ATOM	739 O MET 313 47.2		PROT
30	ATOM	740 N SER 314 48.1		PROT
	ATOM	741 CA SER 314 49.		PROT
	ATOM		399 9.042 20.816 1.00 7 .24 453 9.815 19.619 1.00 10.89	PROT
	ATOM			PROT
25	ATOM	744 C SER 314 48.9		PROT
35	ATOM	745 O SER 314 49.5		PROT
	ATOM	746 N LEU 315 48.0 747 CA LEU 315 47.	628 7.605 24.104 1.00 2.00	PROT
	ATOM		521 8.502 24.671 1.00 2.95	PROT
	ATOM			PROT
40	ATOM		.831 8.096 25.992 1.00 2.00 5.876 7.845 27.072 1.00 2.54	PROT
40	ATOM		1.865 9.182 26.444 1.00 2.00	PROT
	ATOM		07 6.182 23.945 1.00 3.25	PROT
	ATOM			PROT
	ATOM		568 5.253 24.603 1.00 2.00 157 6.010 23.039 1.00 7.28	PROT
45	ATOM		157 6.010 23.039 1.00 7.28 1.588 4.691 22.808 1.00 13.31	
45	ATOM			
	ATOM		.551 4.758 21.693 1.00 11.11 .545 5.872 21.887 1.00 10.55	
	ATOM		.354 5.639 21.012 1.00 10.09	
	ATOM		.131 6.149 21.605 1.00 12.29	
50	ATOM		.955 6.127 20.994 1.00 6.99	
50	ATOM	760 CZ ARG 316 39	.777 0.127 20.774 1.00 0.79	1 101

	ATOM ATOM	761 NH1 ARG 316 762 NH2 ARG 316	38.880 6.608 21.595 1.00 19.32 39.853 5.619 19.778 1.00 17.16	PROT PROT
	ATOM	763 C ARG 316	46.666 3.686 22.458 1.00 10.10	PROT
	ATOM	764 O ARG 316	46.549 2.508 22.753 1.00 14.94	PROT
5	ATOM	765 N ALA 317	47.723 4.148 21.819 1.00 6.51	PROT
,	ATOM	766 CA ALA 317	48.801 3.243 21.474 1.00 11.04	PROT
	ATOM	767 CB ALA 317	49.749 3.902 20.487 1.00 16.13	PROT
	ATOM	768 C ALA 317	49.539 2.910 22.753 1.00 12.70	PROT
	ATOM	769 O ALA 317	49.822 1.755 23.033 1.00 23.09	PROT
10	ATOM	770 N ALA 318	49.832 3.943 23.534 1.00 14.79	PROT
	ATOM	771 CA ALA 318	50.567 3.779 24.776 1.00 8.38	PROT
	ATOM	772 CB ALA 318	50.727 5.122 25.448 1.00 11.75	PROT
	ATOM	773 C ALA 318	49.941 2.786 25.741 1.00 10.30	PROT
	ATOM	774 O ALA 318	50.585 1.824 26.165 1.00 8.48	PROT
15	ATOM	775 N VAL 319	48.680 3.011 26.083 1.00 7.87	PROT
	ATOM	776 CA VAL 319	48.002 2.131 27.027 1.00 9.64	PROT
	ATOM	777 CB VAL 319	46.579 2.622 27.334 1.00 2.57	PROT
	ATOM	778 CG1 VAL 319	46.644 3.929 28.127 1.00 5.09	PROT
	ATOM	779 CG2 VAL 319	45.807 2.823 26.043 1.00 5.15	PROT
20	ATOM	780 C VAL 319	47.930 0.695 26.541 1.00 11.68	PROT
	ATOM	781 O VAL 319	47.440 -0.171 27.254 1.00 16.32	PROT
	ATOM	782 N ARG 320	48.415 0.444 25.329 1.00 16.40	PROT
	ATOM	783 CA ARG 320	48.405 -0.902 24.767 1.00 13.20	PROT
~~	ATOM	784 CB ARG 320	47.736 -0.918 23.393 1.00 2.00	PROT
25	ATOM	785 CG ARG 320	46.310 -0.405 23.420 1.00 14.07	PROT
	ATOM	786 CD ARG 320	45.283 -1.460 23.035 1.00 19.69 44.168 -0.868 22.292 1.00 36.52	PROT PROT
	ATOM	787 NE ARG 320 788 CZ ARG 320	42.912 -1.313 22.322 1.00 47.43	PROT
	ATOM ATOM	789 NH1 ARG 320	41.966 -0.705 21.609 1.00 43.57	
30	ATOM	790 NH2 ARG 320	42.596 -2.367 23.061 1.00 49.93	PROT
50	ATOM	791 C ARG 320	49.835 -1.391 24.662 1.00 15.45	PROT
	ATOM	792 O ARG 320	50.167 -2.218 23.809 1.00 24.78	PROT
	ATOM	793 N TYR 321	50.684 -0.860 25.537 1.00 13.68	PROT
	ATOM	794 CA TYR 321	52.085 -1.258 25.572 1.00 18.80	PROT
35	ATOM	795 CB TYR 321	52.925 -0.208 26.295 1.00 9.64	PROT
	ATOM	796 CG TYR 321	54.313 -0.685 26.622 1.00 11.20	PROT
	ATOM	797 CD1 TYR 321	55.211 -1.005 25.612 1.00 2.00	PROT
	ATOM	798 CE1 TYR 321	56.483 -1.461 25.906 1.00 9.63	PROT
	ATOM	799 CD2 TYR 321	54.727 -0.834 27.943 1.00 18.93	PROT
40	ATOM	800 CE2 TYR 321	56.003 -1.293 28.250 1.00 19.49	PROT
	ATOM	801 CZ TYR 321	56.874 -1.604 27.225 1.00 14.75	PROT
	ATOM	802 OH TYR 321	58.137 -2.053 27.518 1.00 22.96	PROT
	ATOM	803 C TYR 321	52.209 -2.607 26.287 1.00 19.74	PROT
	ATOM	804 O TYR 321	51.483 -2.889 27.242 1.00 31.56	PROT
45	ATOM	805 N ASP 322	53.136 -3.435 25.823 1.00 26.35	PROT
	ATOM	806 CA ASP 322	53.346 -4.759 26.392 1.00 22.38	PROT
	ATOM	807 CB ASP 322	52.982 -5.814 25.353 1.00 33.63	PROT
	ATOM	808 CG ASP 322	52.601 -7.128 25.970 1.00 40.70	PROT
5.0	ATOM	809 OD1 ASP 322	51.539 -7.658 25.591 1.00 48.18	PROT
50	ATOM	810 OD2 ASP 322	53.358 -7.628 26.826 1.00 38.91	PROT

	ATOM	811 C ASP 322	54.800 -4.928 26.776 1.00 23.51	PROT
	ATOM	812 O ASP 322	55.683 -4.844 25.924 1.00 37.80	PROT
	ATOM	813 N PRO 323	55.076 -5.160 28.066 1.00 24.06	PROT
	ATOM	814 CD PRO 323	54.130 -5.258 29.187 1.00 19.35	PROT
5	AŢOM	815 CA PRO 323	56.462 -5.339 28.507 1.00 23.60	PROT
	ATOM	816 CB PRO 323	56.390 -5.121 30.007 1.00 3.90	PROT
	ATOM	817 CG PRO 323	55.031 -5.570 30.360 1.00 14.06	PROT
	ATOM	818 C PRO 323	56.949 -6.736 28.151 1.00 21.79	PROT
	ATOM	819 O PRO 323	58.149 -7.003 28.119 1.00 27.28	PROT
10	ATOM	820 N GLU 324	56.009 -7.633 27.889 1.00 37.63	PROT
	ATOM	821 CA GLU 324	56.366 -8.993 27.524 1.00 42.63	PROT
	ATOM	822 CB GLU 324	55.133 -9.885 27.551 1.00 37.58	PROT
	ATOM	823 C GLU 324	56.971 -8.956 26.124 1.00 43.28	PROT
	ATOM	824 O GLU 324	58.154 -9.239 25.938 1.00 43.14	PROT
15	ATOM	825 N SER 325	56.153 -8.586 25.142 1.00 31.72	PROT
	ATOM	826 CA SER 325	56.607 -8.508 23.765 1.00 30.34	PROT
	ATOM	827 CB SER 325	55.413 -8.522 22.814 1.00 17.63	PROT
	ATOM	828 OG SER 325	54.356 -7.729 23.315 1.00 31.90	PROT
	ATOM	829 C SER 325	57.441 -7.257 23.519 1.00 31.94	PROT
20	ATOM	830 O SER 325	58.146 -7.169 22.513 1.00 45.47	PROT
	ATOM	831 N GLU 326	57.359 -6.289 24.429 1.00 31.10	PROT
	ATOM	832 CA GLU 326	58.119 -5.050 24.281 1.00 31.43	PROT
	ATOM	833 CB GLU 326	59.598 -5.382 24.091 1.00 30.39	PROT
	ATOM	834 CG GLU 326	60.552 -4.342 24.612 1.00 35.00	PROT
25	ATOM	835 CD GLU 326	61.738 -4.965 25.304 1.00 29.12	PROT
	ATOM	836 OE1 GLU 326	61.525 -5.579 26.370 1.00 39.21	PROT
	ATOM	837 OE2 GLU 326	62.872 -4.844 24.788 1.00 29.11	PROT
	ATOM	838 C GLU 326	57.605 -4.283 23.063 1.00 28.37	PROT
	ATOM	839 O GLU 326	58.382 -3.677 22.321 1.00 26.51	PROT
30	ATOM	840 N THR 327	56.290 -4.301 22.873 1.00 23.71	PROT
	ATOM	841 CA THR 327	55.674 -3.648 21.720 1.00 22.11	PROT
	ATOM	842 CB THR 327	55.298 -4.705 20.652 1.00 28.08	PROT
	ATOM	843 OG1 THR 327	54.226 -5.524 21.145 1.00 16.87	PROT
	ATOM	844 CG2 THR 327	56.494 -5.597 20.340 1.00 24.03	PROT
35	ATOM	845 C THR 327	54.420 -2.824 22.046 1.00 22.42	PROT
	ATOM	846 O THR 327	53.928 -2.830 23.172 1.00 17.50	PROT
	ATOM	847 N LEU 328	53.914 -2.122 21.038 1.00 17.28	PROT
	ATOM	848 CA LEU 328	52.728 -1.285 21.171 1.00 14.83	PROT
40	ATOM	849 CB LEU 328	53.065 0.157 20.806 1.00 15.27	PROT
40	ATOM	850 CG LEU 328	53.693 1.036 21.879 1.00 10.50	PROT
	ATOM	851 CD1 LEU 328	54.137 2.336 21.254 1.00 16.75	PROT
	ATOM	852 CD2 LEU 328	52.682 1.285 22.979 1.00 20.19	PROT
	ATOM	853 C LEU 328	51.687 -1.804 20.198 1.00 18.16	PROT
45	ATOM	854 O LEU 328	52.035 -2.508 19.254 1.00 23.88	PROT
45	ATOM	855 N THR 329	50.421 -1.450 20.402 1.00 9.40	PROT
	ATOM	856 CA THR 329	49.389 -1.920 19.495 1.00 8.26	PROT
	ATOM	857 CB THR 329	48.460 -2.888 20.199 1.00 8.67	PROT
	ATOM	858 OG1 THR 329	49.213 -4.052 20.577 1.00 13.23	PROT
50	ATOM	859 CG2 THR 329	47.308 -3.289 19.270 1.00 2.00	PROT
50	ATOM	860 C THR 329	48.569 -0.841 18.800 1.00 16.65	PROT

	ATOM	861 O THR 329	47.726 -0.158 19.406 1.00 17.20	PROT
	ATOM	862 N LEU 330	48.808 -0.725 17.495 1.00 21.56	PROT PROT
	ATOM	863 CA LEU 330	48.138 0.258 16.655 1.00 20.95 49.106 0.676 15.539 1.00 17.36	PROT
_	ATOM	864 CB LEU 330 865 CG LEU 330	49.106 0.676 15.539 1.00 17.36 50.570 0.797 16.028 1.00 12.86	PROT
5	ATOM	865 CG LEU 330 866 CD1 LEU 330	51.531 0.521 14.898 1.00 10.10	PROT
	ATOM ATOM	867 CD2 LEU 330	50.830 2.180 16.600 1.00 2.00	PROT
	ATOM	868 C LEU 330	46.803 -0.258 16.097 1.00 21.35	PROT
	ATOM	869 O LEU 330	46.803 -0.238 16.097 1.00 21.33	PROT
10	ATOM	870 N ASN 331	45.834 0.648 15.987 1.00 27.76	PROT
10	ATOM	871 CA ASN 331	44.487 0.338 15.498 1.00 28.09	PROT
	ATOM	872 CB ASN 331	44.460 0.275 13.971 1.00 24.95	PROT
	ATOM	872 CB ASN 331	43.074 0.540 13.397 1.00 24.55	PROT
	ATOM	874 OD1 ASN 331	42.512 -0.305 12.701 1.00 38.21	PROT
15	ATOM	875 ND2 ASN 331	42.522 1.715 13.680 1.00 24.73	PROT
13	ATOM	876 C ASN 331	43.946 -0.967 16.075 1.00 32.03	PROT
	ATOM	877 O ASN 331	43.166 -1.668 15.431 1.00 35.49	PROT
	ATOM	878 N GLY 332	44.357 -1.282 17.299 1.00 40.24	PROT
	ATOM	879 CA GLY 332	43.894 -2.495 17.941 1.00 38.04	PROT
20	ATOM	880 C GLY 332	44.009 -3.665 16.998 1.00 40.09	PROT
	ATOM	881 O GLY 332	43.001 -4.225 16.563 1.00 45.79	PROT
	ATOM	882 N GLU 333	45.249 -4.013 16.664 1.00 41.60	PROT
	ATOM	883 CA GLU 333	45.539 -5.126 15.763 1.00 36.28	PROT
	ATOM	884 CB GLU 333	44.752 -4.978 14.454 1.00 46.39	PROT
25	ATOM	885 CG GLU 333	44.745 -3.580 13.862 1.00 58.03	PROT
	ATOM	886 CD GLU 333	43.883 -3.485 12.610 1.00 67.00	PROT
	ATOM	887 OE1 GLU 333	44.446 -3.282 11.511 1.00 67.51	PROT
	ATOM	888 OE2 GLU 333	42.644 -3.615 12.727 1.00 71.01	PROT
	ATOM	889 C GLU 333	47.027 -5.266 15.446 1.00 33.13	PROT
30	ATOM	890 O GLU 333	47.563 -6.366 15.486 1.00 27.97	PROT
	ATOM	891 N MET 334	47.692 -4.152 15.143 1.00 27.00	PROT
	ATOM	892 CA MET 334	49.111 -4.188 14.798 1.00 29.83	PROT
	ATOM	893 CB MET 334	49.416 -3.159 13.699 1.00 26.04	PROT
	ATOM	894 CG MET 334	50.561 -3.588 12.765 1.00 28.06	PROT
35	ATOM	895 SD MET 334	51.263 -2.273 11.736 1.00 28.46	PROT
	ATOM	896 CE MET 334	50.021 -2.123 10.497 1.00 22.48	PROT
	ATOM	897 C MET 334	50.087 -3.995 15.959 1.00 33.52	PROT
	ATOM	898 O MET 334	50.071 -2.962 16.631 1.00 35.81	PROT
	ATOM	899 N ALA 335	50.942 -4.996 16.171 1.00 27.46	PROT
40	ATOM	900 CA ALA 335	51.948 -4.976 17.234 1.00 29.69	PROT
	ATOM	901 CB ALA 335	51.966 -6.314 17.965 1.00 12.67	PROT
	ATOM	902 C ALA 335	53.336 -4.682 16.662 1.00 31.74	PROT
	ATOM	903 O ALA 335	53.943 -5.530 16.009 1.00 43.66	PROT
	ATOM	904 N VAL 336	53.848 -3.489 16.923 1.00 23.98	PROT
45	ATOM	905 CA VAL 336	55.151 -3.118 16.405 1.00 21.32	PROT
	ATOM	906 CB VAL 336	55.028 -1.873 15.504 1.00 17.37	PROT
	ATOM	907 CG1 VAL 336	53.945 -2.104 14.462 1.00 14.88	PROT
	ATOM	908 CG2 VAL 336	54.686 -0.648 16.339 1.00 15.53	PROT PROT
50	ATOM	909 C VAL 336	56.150 -2.852 17.526 1.00 22.72	PROT
50	ATOM	910 O VAL 336	55.763 -2.540 18.651 1.00 25.15	LVOI

	ATOM	911 N THR 337	57.435 -3.001 17.220 1.00 19.21	PROT
	ATOM	912 CA THR 337	58.476 -2.765 18.205 1.00 20.31	PROT
	ATOM	913 CB THR 337	59.752 -3.578 17.884 1.00 14.76	PROT
	ATOM	914 OG1 THR 337	59.957 -3.616 16.467 1.00 16.43	PROT
5	ATOM	915 CG2 THR 337	59.615 -4.995 18.393 1.00 7.08	PROT
	ATOM	916 C THR 337	58.785 -1.272 18.157 1.00 24.20	PROT
	ATOM	917 O THR 337	58.322 -0.591 17.245 1.00 28.05	PROT
	ATOM	918 N ARG 338	59.548 -0.766 19.134 1.00 27.55	PROT
	ATOM	919 CA ARG 338	59.917 0.655 19.197 1.00 16.80	PROT
10	ATOM	920 CB ARG 338	60.757 0.942 20.446 1.00 17.04	PROT
_	ATOM	921 CG ARG 338	61.687 2.149 20.303 1.00 9.79	PROT
	ATOM	922 CD ARG 338	62.666 2.276 21.458 1.00 2.00	PROT
	ATOM	923 NE ARG 338	61.994 2.128 22.739 1.00 20.70	PROT
	ATOM	924 CZ ARG 338	61.897 3.083 23.657 1.00 12.04	PROT
15	ATOM	925 NH1 ARG 338	61.261 2.840 24.784 1.00 27.11	PROT
	ATOM	926 NH2 ARG 338	62.436 4.272 23.459 1.00 22.23	PROT
	ATOM	927 C ARG 338	60.702 1.085 17.968 1.00 21.26	PROT
	ATOM	928 O ARG 338	60.338 2.049 17.295 1.00 16.40	PROT
	ATOM	929 N GLY 339	61.792 0.374 17.693 1.00 31.57	PROT
20	ATOM	930 CA GLY 339	62.609 0.696 16.540 1.00 32.42	PROT
_	ATOM	931 C GLY 339	61.816 0.534 15.254 1.00 30.08	PROT
	ATOM	932 O GLY 339	61.932 1.342 14.328 1.00 25.82	PROT
	ATOM	933 N GLN 340	61.008 -0.520 15.192 1.00 16.60	PROT
	ATOM	934 CA GLN 340	60.191 -0.768 14.012 1.00 14.08	PROT
25	ATOM	935 CB GLN 340	59.199 -1.884 14.301 1.00 5.73	PROT
	ATOM	936 CG-GLN 340	58.849 -2.697 13.100 1.00 16.15	PROT
	ATOM	937 CD GLN 340	58.577 -4.141 13.442 1.00 22.46	PROT
	ATOM	938 OE1 GLN 340	57.767 -4.450 14.316 1.00 30.45	PROT
	ATOM	939 NE2 GLN 340	59.254 -5.040 12.749 1.00 34.19	PROT
30	ATOM	940 C GLN 340	59.452 0.521 13.632 1.00 22.07	PROT
	ATOM	941 O GLN 340	59.707 1.103 12.576 1.00 21.13	PROT
	ATOM	942 N LEU 341	58.561 0.976 14.518 1.00 27.88	PROT
	ATOM	943 CA LEU 341	57.778 2.197 14.306 1.00 21.82	PROT
	ATOM	944 CB LEU 341	56.813 2.418 15.483 1.00 10.20	PROT
35	ATOM	945 CG LEU 341	55.930 3.682 15.534 1.00 16.27	PROT
	ATOM	946 CD1 LEU 341	54.777 3.618 14.518 1.00 13.27	PROT
	ATOM	947 CD2 LEU 341	55.370 3.822 16.935 1.00 10.68	PROT
	ATOM	948 C LEU 341	58.683 3.413 14.138 1.00 13.98	PROT
	ATOM	949 O LEU 341	58.315 4.386 13.486 1.00 7.94	PROT
40	ATOM	950 N LYS 342	59.867 3.361 14.734 1.00 11.48	PROT
	ATOM	951 CA LYS 342	60.804 4.465 14.613 1.00 17.77	PROT
	ATOM	952 CB LYS 342	62.063 4.213 15.459 1.00 13.58	PROT
	ATOM	953 CG LYS 342	63.219 5.173 15.140 1.00 13.27	PROT
	ATOM	954 CD LYS 342	64.173 5.358 16.319 1.00 5.44	PROT
45	ATOM	955 CE LYS 342	64.500 6.829 16.546 1.00 5.47	PROT
•	ATOM	956 NZ LYS 342	65.721 7.019 17.388 1.00 4.98	PROT
	ATOM	957 C LYS 342	61.184 4.579 13.141 1.00 19.97	PROT
	ATOM	958 O LYS 342	60.939 5.595 12.501 1.00 20.34	PROT
	ATOM	959 N ASN 343	61.764 3.510 12.605 1.00 26.88	PROT
50	ATOM	960 CA ASN 343	62.196 3.470 11.219 1.00 22.34	PROT

	ATOM	961 CB ASN 343	62.829 2.123 10.929 1.00 4.80	PROT
	ATOM	962 CG ASN 343	64.060 1.894 11.758 1.00 18.77	PROT
	ATOM	963 OD1 ASN 343	64.755 2.848 12.117 1.00 14.12	PROT
	ATOM	964 ND2 ASN 343	64.340 0.634 12.083 1.00 12.72	PROT
5	ATOM	965 C ASN 343	61.091 3.736 10.224 1.00 20.40	PROT
	ATOM	966 O ASN 343	61.309 4.417 9.232 1.00 20.76	PROT
	ATOM	967 N GLY 344	59.908 3.200 10.494 1.00 12.62	PROT
	ATOM	968 CA GLY 344	58.775 3.382 9.603 1.00 6.27	PROT
	ATOM	969 C GLY 344	58.229 4.796 9.451 1.00 14.56	PROT
10	ATOM	970 O GLY 344	57.177 4.972 8.826 1.00 13.30	PROT
	ATOM	971 N GLY 345	58.902 5.795 10.030 1.00 16.51	PROT
	ATOM	972 CA GLY 345	58.439 7.166 9.869 1.00 20.04	PROT
	ATOM	973 C GLY 345	58.248 8.112 11.046 1.00 25.64	PROT
	ATOM	974 O GLY 345	58.243 9.331 10.849 1.00 23.32	PROT
15	ATOM	975 N LEU 346	58.099 7.588 12.260 1.00 22.22	PROT
	ATOM	976 CA LEU 346	57.874 8.449 13.415 1.00 14.94	PROT
	ATOM	977 CB LEU 346	57.070 7.700 14.474 1.00 3.92	PROT
	ATOM	978 CG LEU 346	55.566 7.538 14.193 1.00 5.92	PROT
	ATOM	979 CD1 LEU 346	54.938 6.796 15.355 1.00 2.00	PROT
20	ATOM	980 CD2 LEU 346	54.884 8.885 13.973 1.00 2.00	PROT
	ATOM	981 C LEU 346	59.126 9.042 14.041 1.00 14.60	PROT
	ATOM	982 O LEU 346	59.102 10.153 14.554 1.00 17.36	PROT
	ATOM	983 N GLY 347	60.226 8.312 14.001 1.00 12.09	PROT
	ATOM	984 CA GLY 347	61.455 8.828 14.581 1.00 15.62	PROT
25	ATOM	985 C GLY 347	61.439 8.963 16.090 1.00 6.31	PROT
	ATOM	986 O GLY 347	60.865 8.141 16.790 1.00 13.15	PROT
	ATOM	987 N VAL 348	62.076 10.011 16.592 1.00 13.74	PROT
	ATOM	988 CA VAL 348	62.141 10.259 18.030 1.00 10.13	PROT
	ATOM	989 CB VAL 348	62.757 11.646 18.342 1.00 9.26	PROT
30	ATOM	990 CG1 VAL 348	61.867 12.752 17.794 1.00 2.00	PROT
	ATOM	991 CG2 VAL 348	62.942 11.802 19.836 1.00 2.00	PROT
	ATOM	992 C VAL 348	60.763 10.216 18.650 1.00 6.61	PROT
	ATOM	993 O VAL 348	60.619 10.066 19.862 1.00 3.12	PROT
	ATOM	994 N VAL 349	59.746 10.358 17.816 1.00 5.51	PROT
35	ATOM	995 CA VAL 349	58.386 10.342 18.306 1.00 2.00	PROT
	ATOM	996 CB VAL 349	57.421 10.886 17.260 1.00 4.46	PROT
	ATOM	997 CG1 VAL 349	56.001 10.578 17.656 1.00 2.00	PROT
	ATOM	998 CG2 VAL 349	57.623 12.387 17.122 1.00 2.00	PROT
40	ATOM	999 C VAL 349	57.995 8.933 18.687 1.00 9.15	PROT
40	ATOM	1000 O VAL 349	57.284 8.726 19.664 1.00 15.02	PROT
	ATOM	1001 N SER 350	58.446 7.943 17.933 1.00 7.42	PROT
	ATOM	1002 CA SER 350	58.087 6.590 18.315 1.00 12.87	PROT
	ATOM	1003 CB SER 350	58.695 5.561 17.382 1.00 9.48	PROT
	ATOM	1004 OG SER 350	58.529 4.269 17.931 1.00 10.82	PROT
45	ATOM	1005 C SER 350	58.628 6.364 19.717 1.00 15.55	PROT
	ATOM	1006 O SER 350	57.963 5.761 20.558 1.00 25.88	PROT
	ATOM	1007 N ASP 351	59.838 6.863 19.950 1.00 16.38	PROT
	ATOM	1008 CA ASP 351	60.522 6.743 21.230 1.00 9.58 61.861 7.469 21.176 1.00 7.32	PROT PROT
50	ATOM	1009 CB ASP 351		
50	ATOM	1010 CG ASP 351	62.989 6.576 20.742 1.00 24.16	PROT

	ATOM		7.110 20.275 1.00 30.24	PROT
	ATOM	1012 OD2 ASP 351 62.866	5 5.343 20.869 1.00 33.85	PROT
	ATOM	1013 C ASP 351 59.695	7.360 22.334 1.00 17.01	PROT
•	ATOM	1014 O ASP 351 59.605	6.822 23.435 1.00 26.28	PROT
5	ATOM	1015 N ALA 352 59.100	8.508 22.032 1.00 13.51	PROT
	ATOM	1016 CA ALA 352 58.294	9.224 23.004 1.00 5.19	PROT
	ATOM	1017 CB ALA 352 57.914	10.593 22.452 1.00 2.00	PROT
	ATOM	1018 C ALA 352 57.055	8.432 23.374 1.00 2.00	PROT
	ATOM	1019 O ALA 352 56.701	8.360 24.535 1.00 7.20	PROT
10	ATOM	1020 N ILE 353 56.396		PROT
	ATOM	1021 CA ILE 353 55.201	7.049 22.677 1.00 5.90	PROT
	ATOM		6.626 21.381 1.00 5.87	PROT
	ATOM		6.049 21.732 1.00 2.00	PROT
	ATOM	1024 CG1 ILE 353 54.349		PROT
15	ATOM		7.664 19.294 1.00 2.00	PROT
	ATOM		5.795 23.484 1.00 12.46	PROT
	ATOM		5.426 24.428 1.00 11.74	PROT
	ATOM		5.131 23.122 1.00 19.57	PROT
	ATOM		3.944 23.862 1.00 14.42	PROT
20	ATOM	1030 CB PHE 354 58.256		PROT
	ATOM		2.141 22.284 1.00 9.42	PROT
	ATOM		7 2.401 20.995 1.00 12.33	PROT
	ATOM		2 0.822 22.727 1.00 15.63	PROT
	ATOM		2 1.366 20.165 1.00 6.67	PROT
25	ATOM		3 -0.224 21.900 1.00 16.53	PROT
	ATOM		0.053 20.620 1.00 11.61	PROT
	ATOM	and the second s	4.346 25.307 1.00 18.55	PROT
	ATOM	1038 O PHE 354 56.796	3.740 26.233 1.00 16.67	PROT
20	ATOM	1039 N ASP 355 58.125	5.392 25.491 1.00 12.83	PROT
30	ATOM		5.881 26.818 1.00 5.31	PROT PROT
	ATOM	1041 CB ASP 355 59.351		PROT
	ATOM	1042 CG ASP 355 60.805 1043 OD1 ASP 355 61.112	2 5.683 26.016 1.00 8.53	PROT
	ATOM ATOM	1044 OD2 ASP 355 61.650		PROT
35	ATOM		6.199 27.659 1.00 10.27	PROT
33	ATOM	1045 C ASP 355 57.231	5.972 28.871 1.00 21.86	PROT
	ATOM	1040 O ASI 333 37.231 1047 N LEU 356 56.224	6.726 27.014 1.00 4.18	PROT
	ATOM	1047 N LEO 330 30:224 1048 CA LEU 356 54.988		PROT
	ATOM	1049 CB LEU 356 54.086		PROT
40	ATOM	1050 CG LEU 356 52.694		PROT
40	ATOM	1051 CD1 LEU 356 52.77		PROT
	ATOM	1052 CD2 LEU 356 51.87		PROT
	ATOM	1052 CD2 EEO 350 51.07	5.786 28.091 1.00 9.17	PROT
	ATOM	1054 O LEU 356 53.831	5.644 29.221 1.00 14.77	PROT
45	ATOM	1055 N GLY 357 54.183		PROT
	ATOM		5 3.597 27.413 1.00 6.91	PROT
	ATOM	1057 C GLY 357 54.113	2.879 28.598 1.00 8.33	PROT
	ATOM	1058 O GLY 357 53.400		PROT
	ATOM	1059 N MET 358 55.435		PROT
50	ATOM		2 2:091 29.692 1.00 10.53	PROT
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	ATOM	1061 CB MET 358	57.626 2.153 29.498 1.00 5.45	PROT
	ATOM	1062 CG MET 358	58.138 1.507 28.210 1.00 15.15	PROT
	ATOM	1063 SD MET 358	59.971 1.352 28.113 1.00 17.63	PROT
	ATOM	1064 CE MET 358	60.445 3.023 27.774 1.00 20.56	PROT
5	ATOM	1065 C MET 358	55.714 2.809 30.972 1.00 15.08	PROT
	ATOM	1066 O MET 358	55.241 2.191 31.920 1.00 27.69	PROT
	ATOM	1067 N SER 359	55.875 4.125 30.984 1.00 20.67	PROT
	ATOM	1068 CA SER 359	55.551 4.924 32.158 1.00 19.72	PROT
	ATOM	1069 CB SER 359	55.831 6.398 31.861 1.00 19.98	PROT
10	ATOM	1070 OG SER 359	54.753 7.220 32.262 1.00 33.66	PROT
	ATOM	1071 C SER 359	54.115 4.757 32.656 1.00 22.67	PROT
	ATOM	1072 O SER 359	53.849 4.837 33.860 1.00 22.94	PROT
	ATOM	1073 N LEU 360	53.197 4.514 31.727 1.00 20.55	PROT
	ATOM	1074 CA LEU 360	51.785 4.360 32.054 1.00 17.01	PROT
15	ATOM	1075 CB LEU 360	50.934 4.578 30.802 1.00 2.60	PROT
	ATOM	1076 CG LEU 360	50.674 5.988 30.291 1.00 6.99	PROT
	ATOM	1077 CD1 LEU 360	49.589 5.935 29.236 1.00 4.15	PROT
	ATOM	1078 CD2 LEU 360	50.247 6.892 31.432 1.00 18.93	PROT
	ATOM	1079 C LEU 360	51.437 3.001 32.638 1.00 19.29	PROT
20	ATOM	1080 O LEU 360	50.319 2.802 33.102 1.00 27.53	PROT
	ATOM	1081 N SER 361	52.375 2.061 32.596 1.00 21.73	PROT
	ATOM	1082 CA SER 361	52.139 0.712 33.114 1.00 23.03	PROT
	ATOM	1083 CB SER 361	53.415 -0.130 33.027 1.00 25.89	PROT
	ATOM	1084 OG SER 361	53.645 -0.613 31.717 1.00 27.77	PROT
25	ATOM	1085 C SER 361	51.681 0.730 34.563 1.00 23.26	PROT
	ATOM	1086 O SER 361	50.720 0.046 34.929 1.00 18.73	PROT
	ATOM	1087 N SER 362	52.388 1.524 35.367 1.00 29.84	PROT
	ATOM	1088 CA SER 362	52.141 1.668 36.799 1.00 24.49	PROT
	ATOM	1089 CB SER 362	53.435 2.089 37.491 1.00 26.14	PROT
30	ATOM	1090 OG SER 362	53.917 3.305 36.949 1.00 25.03	PROT
	ATOM	1091 C SER 362	51.031 2.635 37.210 1.00 26.86	PROT
	ATOM	1092 O SER 362	50.797 2.831 38.404 1.00 39.63	PROT
	ATOM	1093 N PHE 363	50.361 3.251 36.240 1.00 20.94	PROT
	ATOM	1094 CA PHE 363	49.272 4.185 36.545 1.00 18.33	PROT PROT
35	ATOM	1095 CB PHE 363	49.191 5.294 35.486 1.00 17.03	
	ATOM	1096 CG PHE 363	50.171 6.407 35.706 1.00 22.73	PROT PROT
	ATOM	1097 CD1 PHE 363	49.733 7.689 35.990 1.00 9.72	
	ATOM	1098 CD2 PHE 363	51.545 6.167 35.659 1.00 24.77	PROT
40	ATOM	1099 CE1 PHE 363	50.645 8.712 36.225 1.00 16.85	PROT
40	ATOM	1100 CE2 PHE 363	52.463 7.198 35.897 1.00 14.26	PROT
	ATOM	1101 CZ PHE 363	52.011 8.462 36.179 1.00 2.26	PROT
	ATOM	1102 C PHE 363	47.958 3.417 36.598 1.00 16.57	PROT
	ATOM	1103 O PHE 363	46.971 3.882 37.165 1.00 13.08	PROT
	ATOM	1104 N ASN 364	47.976 2.231 36.002 1.00 17.31	PROT
45	ATOM	1105 CA ASN 364	46.819 1.349 35.949 1.00 26.11	PROT
	ATOM	1106 CB ASN 364	46.673 0.608 37.276 1.00 16.96	PROT
	ATOM	1107 CG ASN 364		PROT
	ATOM	1108 OD1 ASN 364		PROT
	ATOM	1109 ND2 ASN 364		PROT
50	ATOM	1110 C ASN 364	45.527 2.060 35.594 1.00 18.22	PROT

	ATOM	1111 O ASN 364	44.522 1.923 36.286 1.00 23.17	PROT
	ATOM	1112 N LEU 365	45.567 2.803 34.491 1.00 13.10	PROT
	ATOM	1113 CA LEU 365	44.417 3.562 34.013 1.00 15.41	PROT
	ATOM	1114 CB LEU 365	44.833 4.483 32.861 1.00 16.55	PROT
5	ATOM	1115 CG LEU 365	45.762 5.653 33.181 1.00 19.56	PROT
•	ATOM	1116 CD1 LEU 365	46.146 6.373 31.897 1.00 6.69	PROT
	ATOM	1117 CD2 LEU 365	45.067 6.602 34.128 1.00 15.69	PROT
	ATOM	1118 C LEU 365	43.328 2.624 33.520 1.00 12.07	PROT
	ATOM	1119 O LEU 365	43.620 1.534 33.043 1.00 19.81	PROT
10	ATOM	1120 N ASP 366	42.077 3.047 33.653 1.00 10.86	PROT
	ATOM	1121 CA ASP 366	40.942 2.263 33.180 1.00 8.96	PROT
	ATOM	1122 CB ASP 366	39.933 2.021 34.326 1.00 9.59	PROT
	ATOM	1123 CG ASP 366	39.300 3.306 34.859 1.00 21.78	PROT
	ATOM	1124 OD1 ASP 366	39.871 4.397 34.676 1.00 25.60	PROT
15	ATOM	1125 OD2 ASP 366	38.217 3.222 35.474 1.00 19.16	PROT
• •	ATOM	1126 C ASP 366	40.288 3.005 32.002 1.00 8.82	PROT
	ATOM	1127 O ASP 366	40.666 4.132 31.681 1.00 17.66	PROT
	ATOM	1128 N ASP 367	39.321 2.379 31.346 1.00 9.45	PROT
	ATOM	1129 CA ASP 367	38.668 3.023 30.218 1.00 11.11	PROT
20	ATOM	1130 CB ASP 367	37.457 2.205 29.769 1.00 20.67	PROT
	ATOM	1131 CG ASP 367	37.832 0.812 29.301 1.00 25.02	PROT
	ATOM	1132 OD1 ASP 367	39.040 0.525 29.158 1.00 21.06	PROT
	ATOM	1133 OD2 ASP 367	36.909 0.002 29.076 1.00 31.37	PROT
	ATOM	1134 C ASP 367	38.233 4.445 30.574 1.00 14.44	PROT
25	ATOM	1135 O ASP 367	38.457 5.380 29.815 1.00 26.42	PROT
	ATOM	1136 N THR 368	37.619 4.612 31.735 1.00 13.62	PROT
	ATOM	1137 CA THR 368	37.157 5.926 32.160 1.00 13.14	PROT
	ATOM	1138 CB THR 368	36.510 5.853 33.547 1.00 16.53	PROT
	ATOM	1139 OG1 THR 368	35.482 4.856 33.550 1.00 10.44	PROT
30	ATOM	1140 CG2 THR 368	35.928 7.188 33.925 1.00 5.20	PROT
	ATOM	1141 C THR 368	38.291 6.942 32.226 1.00 13.03	PROT
	ATOM	1142 O THR 368	38.114 8.108 31.878 1.00 12.90	PROT
	ATOM	1143 N GLU 369	39.455 6.492 32.686 1.00 9.96	PROT
	ATOM	1144 CA GLU 369	40.616 7.365 32.821 1.00 7.34	PROT
35	ATOM	1145 CB GLU 369	41.673 6.687 33.708 1.00 10.25	PROT
	ATOM	1146 CG GLU 369	41:584 7.113 35.189 1.00 14.56	PROT
	ATOM	1147 CD GLU 369	41.599 5.945 36.167 1.00 19.39	PROT
	ATOM	1148 OE1 GLU 369	42.255 4.922 35.864 1.00 19.65	PROT
	ATOM	1149 OE2 GLU 369	40.954 6.054 37.233 1.00 7.98	PROT
40	ATOM	1150 C GLU 369	41.203 7.768 31.468 1.00 4.33	PROT
	ATOM	1151 O GLU 369	41.467 8.944 31.213 1.00 7.50	PROT
	ATOM	1152 N VAL 370	41.406 6.784 30.603 1.00 12.29	PROT
	ATOM	1153 CA VAL 370	41.927 7.040 29.267 1.00 19.01	PROT
	ATOM	1154 CB VAL 370	42.092 5.726 28.496 1.00 10.10	PROT
45	ATOM	1155 CG1 VAL 370	42.431 6.011 27.049 1.00 8.57	PROT
. =	ATOM	1156 CG2 VAL 370	43.168 4.877 29.159 1.00 12.40	PROT
	ATOM	1157 C VAL 370	40.896 7.915 28.555 1.00 18.30	PROT
	ATOM	1158 O VAL 370	41.230 8.872 27.855 1.00 17.19	PROT
	ATOM	1159 N ALA 371	39.633 7.581 28.760 1.00 2.00	PROT
50	ATOM	1160 CA ALA 371	38.549 8.321 28.157 1.00 3.53	PROT

	ATOM		37.215 7.728 28.591 1.00 9.17	PROT
	ATOM	1162 C ALA 371	38.603 9.797 28.529 1.00 9.97	PROT
	ATOM	1163 O ALA 371	38.626 10.666 27.655 1.00 24.55	PROT
	ATOM	1164 N LEU 372	38.633 10.082 29.831 1.00 14.85	PROT
5	ATOM	1165 CA LEU 372	38.636 11.463 30.307 1.00 9.24	PROT
	ATOM	1166 CB LEU 372	38.480 11.501 31.830 1.00 8.83	PROT
	ATOM	1167 CG LEU 372	37.043 11.288 32.364 1.00 5.50	PROT
	ATOM		37.036 10.338 33.553 1.00 2.02	PROT
	ATOM		36.455 12.626 32.770 1.00 2.00	PROT
10	ATOM		39.867 12.218 29.870 1.00 10.17	PROT
	ATOM		39.791 13.413 29.568 1.00 7.23	PROT
	ATOM		40.996 11.510 29.825 1.00 13.10	PROT
	ATOM		42.270 12.078 29.399 1.00 2.00	PROT
	ATOM		43.325 10.981 29.381 1.00 2.00	PROT
15	ATOM		44.705 11.118 30.045 1.00 9.64	PROT
	ATOM		44.817 12.382 30.875 1.00 2.00	PROT
	ATOM		44.955 9.883 30.882 1.00 2.00	PROT
	ATOM	1178 C LEU 373	42.026 12.602 27.987 1.00 6.58	PROT
20	ATOM	1179 O LEU 373	42.357 13.738 27.660 1.00 9.73	PROT
20	ATOM	1180 N GLN 374	41.401 11.763 27.165 1.00 9.45 41.076 12.097 25.785 1.00 2.00	PROT PROT
	ATOM	1181 CA GLN 374	40.382 10.914 25.121 1.00 2.00	PROT
	ATOM	1182 CB GLN 374 1183 CG GLN 374	41.332 9.896 24.537 1.00 2.00	PROT
	ATOM	1184 CD GLN 374	40.630 8.641 24.095 1.00 2.00	PROT
25	ATOM	1185 OEI GLN 374	41.261 7.622 23.855 1.00 8.01	PROT
23	ATOM	1186 NE2 GLN 374	39.316 8.705 23.989 1.00 2.00	PROT
	ATOM	1187 C GLN 374	40.187 13.326 25.694 1.00 2.78	PROT
	ATOM	1188 O GLN 374	40.427 14.213 24.875 1.00 13.91	PROT
	ATOM	1189 N ALA 375	39.151 13.386 26.521 1.00 2.00	PROT
30	ATOM	1190 CA ALA 375	38.261 14.546 26.505 1.00 2.00	PROT
50	ATOM	1191 CB ALA 375	37.128 14.348 27.489 1.00 3.97	PROT
	ATOM	1192 C ALA 375	39.061 15.801 26.868 1.00 4.60	PROT
	ATOM	1193 O ALA 375	38.881 16.864 26.274 1.00 8.82	PROT
	ATOM	1194 N VAL 376	39.956 15.667 27.842 1.00 9.01	PROT
35	ATOM	1195 CA VAL 376	40.772 16.790 28.267 1.00 7.36	PROT
	ATOM	1196 CB VAL 376	41.669 16.401 29.467 1.00 2.30	PROT
	ATOM	1197 CG1 VAL 376	42.597 17.532 29.839 1.00 2.00	PROT
	ATOM	1198 CG2 VAL 376	40.801 16.076 30.646 1.00 9.15	PROT
	ATOM	1199 C VAL 376	41.629 17.256 27.110 1.00 3.94	PROT
40	ATOM	1200 O VAL 376	41.788 18.455 26.880 1.00 2.00	PROT
	ATOM	1201 N LEU 377	42.179 16.297 26.379 1.00 3.92	PROT
	ATOM	1202 CA LEU 377	43.020 16.618 25.239 1.00 5.65	PROT
	ATOM	1203 CB LEU 377	43.714 15.354 24.731 1.00 5.08	PROT
	ATOM	1204 CG LEU 377	45.052 15.005 25.386 1.00 2.00	PROT
45	ATOM	1205 CD1 LEU 377	45.620 13.790 24.719 1.00 2.00	PROT
	ATOM	1206 CD2 LEU 377	46.016 16.157 25.264 1.00 4.14	PROT
	ATOM	1207 C LEU 377	42.173 17.271 24.137 1.00 11.35	PROT
	ATOM	1208 O LEU 377	42.607 18.240 23.515 1.00 8.78	PROT
	ATOM	1209 N LEU 378	40.959 16.766 23.912 1.00 5.62	PROT
50	ATOM	1210 CA LEU 378	40.080 17.352 22.900 1.00 8.57	PROT

	ATOM	1211 CB LEU 378		PROT
	ATOM	1212 CG LEU 378	37.847 16.993 21.658 1.00 6.60	PROT
	ATOM	1213 CD1 LEU 378	38.550 16.826 20.329 1.00 2.00	PROT
	ATOM	1214 CD2 LEU 378	36.563 16.172 21.690 1.00 9.27	PROT
5	ATOM	1215 C LEU 378	39.738 18.833 23.146 1.00 10.76	PROT
	ATOM	1216 O LEU 378	40.045 19.689 22.312 1.00 14.81	PROT
	ATOM	1217 N MET 379	39.106 19.139 24.278 1.00 13.15	PROT
	ATOM	1218 CA MET 379	38.735 20.521 24.591 1.00 13.60	PROT
	ATOM	1219 CB MET 379	37.698 20.543 25.709 1.00 12.57	PROT
10	ATOM	1220 CG MET 379	36.425 19.782 25.395 1.00 21.12	PROT
	ATOM	1221 SD MET 379	35.533 20.396 23.927 1.00 15.79	PROT
	ATOM	1222 CE MET 379	34.397 19.099 23.756 1.00 13.95	
	ATOM	1223 C MET 379	39.912 21.419 24.988 1.00 16.01	PROT
	ATOM	1224 O MET 379	39.981 21.897 26.121 1.00 16.95	PROT
15	ATOM	1225 N SER 380	40.824 21.663 24.048 1.00 12.39	PROT
	ATOM	1226 CA SER 380	41.984 22.506 24.303 1.00 10.77	PROT
	ATOM	1227 CB SER 380	43.248 21.815 23.810 1.00 8.45	PROT
	ATOM	1228 OG SER 380	43.288 20.487 24.286 1.00 17.27	PROT
	ATOM	1229 C SER 380	41.825 23.859 23.621 1.00 15.58	PROT
20	ATOM	1230 O SER 380	42.125 24.019 22.432 1.00 23.09	PROT
	ATOM	1231 N SER 381	41.368 24.837 24.396 1.00 23.65	PROT
	ATOM	1232 CA SER 381	41.123 26.187 23.904 1.00 25.18	PROT
	ATOM	1233 CB SER 381	40.449 27.018 25.003 1.00 34.78	PROT
	ATOM	1234 OG SER 381	41.250 27.073 26.170 1.00 37.79	PROT
25	ATOM	1235 C SER 381	42.342 26.940 23.388 1.00 19.38	PROT
	ATOM	1236 O SER 381	42.216 28.032 22.850 1.00 28.81	PROT
	ATOM	1237 N ASP 382	43.519 26.361 23.523 1.00 11.80	PROT
	ATOM	1238 CA ASP 382	44.716 27.057 23.082 1.00 15.78	PROT
	ATOM	1239 CB ASP 382	45.908 26.595 23.909 1.00 33.97	PROT
30	ATOM	1240 CG ASP 382	46.069 25.098 23.891 1.00 48.78	PROT
	ATOM	1241 OD1 ASP 382	45.169 24.401 24.406 1.00 45.58	PROT
	ATOM	1242 OD2 ASP 382	47.091 24.620 23.356 1.00 56.52	PROT
	ATOM	1243 C ASP 382	45.037 26.888 21.604 1.00 21.28	PROT
	ATOM	1244 O ASP 382	45.907 27.585 21.079 1.00 41.91	PROT
35	ATOM	1245 N ARG 383	44.357 25.971 20.923 1.00 21.81	PROT
	ATOM	1246 CA ARG 383	44.636 25.773 19.503 1.00 18.95	PROT
		1247 CB ARG 383	· = · · · ·	PROT
		1248 CG ARG 383	43.580 23.491 19.821 1.00 18.07	PROT
40		1249 CD ARG 383	44.693 22.487 19.610 1.00 11.10	PROT
40		1250 NE ARG 383		PROT
		1251 CZ ARG 383	45.460 20.462 20.786 1.00 18.25	PROT
	ATOM		45.187 19.365 21.481 1.00 5.24	PROT
	ATOM		46.717 20.765 20.495 1.00 19.21	PROT
4.0	ATOM		44.420 27.064 18.728 1.00 19.64	PROT
45	ATOM		43.493 27.828 19.001 1.00 17.46	PROT
	ATOM		45.298 27.342 17.762 1.00 25.37	PROT
	ATOM		46.485 26.567 17.359 1.00 35.06	PROT
	ATOM		45.124 28.569 16.983 1.00 27.53	PROT
50	ATOM		46.422 28.693 16.181 1.00 18.75 47.041 27.338 16.190 1.00 27.78	PROT PROT
50	ATOM	1260 CG PRO 384	47.041 27.330 10.190 1.00 27.78	LVOI

	ATOM	1261 C PRO 384	43.895 28.476 16.081 1.00 28.76	PROT
	ATOM	1262 O PRO 384	43.562 27.402 15.560 1.00 31.18	PROT
	ATOM	1263 N GLY 385	43.215 29.606 15.917 1.00 27.37	PROT
	ATOM	1264 CA GLY 385	42.039 29.638 15.073 1.00 26.98	PROT
5	ATOM	1265 C GLY 385	40.728 29.442 15.803 1.00 27.46	PROT
•	ATOM	1266 O GLY 385	39.689 29.911 15.339 1.00 31.99	PROT
	ATOM	1267 N LEU 386	40.756 28.756 16.939 1.00 34.99	PROT
	ATOM	1268 CA LEU 386	39.524 28.515 17.673 1.00 37.24	PROT
	ATOM	1269 CB LEU 386	39.820 27.947 19.059 1.00 26.60	PROT
10	ATOM	1270 CG LEU 386	40.233 26.472 18.988 1.00 32.45	PROT
	ATOM	1271 CD1 LEU 386	40.177 25.859 20.363 1.00 34.82	PROT
	ATOM	1272 CD2 LEU 386	39.314 25.719 18.030 1.00 29.64	PROT
	ATOM	1273 C LEU 386	38.733 29.795 17.778 1.00 36.93	PROT
	ATOM	1274 O LEU 386	39.291 30.881 17.674 1.00 37.60	PROT
15	ATOM	1275 N ALA 387	37.427 29.665 17.962 1.00 31.47	PROT
	ATOM	1276 CA ALA 387	36.578 30.832 18.058 1.00 28.80	PROT
	ATOM	1277 CB ALA 387	35.553 30.814 16.950 1.00 41.01	PROT
	ATOM	1278 C ALA 387	35.890 30.864 19.400 1.00 28.89	PROT
	ATOM	1279 O ALA 387	35.998 31.842 20.133 1.00 30.62	PROT
20	ATOM	1280 N CYS 388	35.167 29.797 19.710 1.00 25.92	PROT
	ATOM	1281 CA CYS 388	34.469 29.712 20.978 1.00 26.90	PROT
	ATOM	1282 CB CYS 388	33.224 28.823 20.826 1.00 21.38	PROT
	ATOM	1283 SG CYS 388	31.625 29.732 20.698 1.00 33.66	PROT
	ATOM	1284 C CYS 388	35.443 29.159 22.040 1.00 31.18	PROT
25	ATOM	1285 O CYS 388	35.272 28.054 22.552 1.00 36.57	PROT
	ATOM	1286 N VAL 389	36.473 29.951 22.346 1.00 20.22	PROT
	ATOM	1287 CA VAL 389	37.511 29.622 23.327 1.00 16.02	PROT
	ATOM	1288 CB VAL 389	38.554 30.737 23.381 1.00 9.80	PROT
	ATOM	1289 CG1 VAL 389	39.526 30.480 24.498 1.00 16.03	PROT
30	ATOM	1290 CG2 VAL 389	39.257 30.843 22.056 1.00 16.27	PROT
	ATOM	1291 C VAL 389	36.977 29.425 24.753 1.00 18.85	PROT
	ATOM	1292 O VAL 389	37.066 28.336 25.323 1.00 24.21	PROT
	ATOM	1293 N GLU 390	36.461 30.500 25.337 1.00 5.06	PROT
	ATOM	1294 CA GLU 390	35.908 30.434 26.660 1.00 2.00	PROT
35	ATOM	1295 CB GLU 390	35.092 31.684 26.952 1.00 5.13	PROT Prot
	ATOM	1296 C GLU 390	35.047 29.184 26.817 1.00 3.75 35.252 28.419 27.754 1.00 23.35	PROT
	ATOM	1297 O GLU 390	35.252 28.419 27.734 1.00 25.53 34.103 28.938 25.915 1.00 14.06	PROT
	ATOM	1298 N ARG 391	33.248 27.754 26.093 1.00 26.18	PROT
40	ATOM	1299 CA ARG 391	32.121 27.699 25.049 1.00 31.84	PROT
40	ATOM	1300 CB ARG 391	30.843 27.040 25.601 1.00 47.73	PROT
	ATOM	1301 CG ARG 391 1302 CD ARG 391	29.882 26.572 24.512 1.00 58.24	PROT
	ATOM		29.882 20.372 24.312 1.00 36.24 29.879 27.487 23.378 1.00 66.80	PROT
	ATOM	1303 NE ARG 391 1304 CZ ARG 391	29.001 28.470 23.211 1.00 69.56	PROT
15	ATOM	1304 CZ ARG 391 1305 NH1 ARG 391	29.088 29.255 22.139 1.00 66.99	PROT
45	ATOM	1306 NH2 ARG 391	28.034 28.663 24.105 1.00 56.08	
	ATOM ATOM	1306 NH2 ARG 391 1307 C ARG 391	33.979 26.415 26.110 1.00 23.65	PROT
	ATOM	1307 C ARG 391 1308 O ARG 391	33.561 25.479 26.794 1.00 28.58	PROT
	ATOM	1309 N ILE 392	35.064 26.316 25.359 1.00 15.05	PROT
50	ATOM	1310 CA ILE 392	35.812 25.077 25.335 1.00 19.03	PROT
20	A I OIVI	ISTO CA ILL 372	JJ.012 2J.011 2J.JJJ 1.00 17.0J	

		1311 CB ILE 392	36.804 25.063 24.165 1.00 22.30 37.971 24.130 24.467 1.00 21.71	PROT PROT
		1312 CG2 ILE 392		
		1313 CG1 ILE 392	36.074 24.614 22.892 1.00 23.47	PROT
_		1314 CD1 ILE 392	36.245 25.551 21.707 1.00 4.13	PROT
5				PROT
			36.728 23.783 27.153 1.00 26.11	PROT
		1317 N GLU 393	36.947 26.029 27.266 1.00 30.74	PROT
		1318 CA GLU 393	37.630 26.021 28.558 1.00 23.39	PROT
		1319 CB GLU 393	38.073 27.430 28.930 1.00 27.18	PROT
10		1320 CG GLU 393	39.435 27.817 28.402 1.00 41.39	PROT
		1321 CD GLU 393	39.990 29.051 29.093 1.00 47.72	PROT
		1322 OE1 GLU 393	39.365 29.524 30.070 1.00 39.94 41.051 29.547 28.653 1.00 51.17	PROT
		1323 OE2 GLU 393		PROT
		1324 C GLU 393	36.655 25.516 29.610 1.00 21.72 36.942 24.574 30.344 1.00 22.82	PROT
15		1325 O GLU 393		PROT
		1326 N LYS 394	35.497 26.163 29.676 1.00 9.64 34.462 25.779 30.618 1.00 11.56	PROT PROT
		1327 CA LYS 394		
		1328 CB LYS 394	33.177 26.557 30.338 1.00 7.52	PROT
20	ATOM	1329 C LYS 394	34.213 24.280 30.492 1.00 16.31	PROT
20	ATOM	1330 O LYS 394	34.000 23.594 31.498 1.00 24.52	PROT PROT
	ATOM	1331 N TYR 395	34.251 23.763 29.264 1.00 12.79	
	ATOM	1332 CA TYR 395	34.033 22.332 29.057 1.00 19.02	PROT
	ATOM	1333 CB TYR 395	33.803 22.025 27.572 1.00 27.90	PROT
0.5	ATOM	1334 CG TYR 395	32.454 22.456 27.027 1.00 31.64	PROT
25	ATOM	1335 CD1 TYR 395	32.136 22.267 25.684 1.00 30.15	PROT PROT
	ATOM	1336 CE1 TYR 395	30.927 22.695 25.160 1.00 28.34	PROT
	ATOM	1337 CD2 TYR 395	31.514 23.085 27.835 1.00 34.21	PROT
	ATOM	1338 CE2 TYR 395	30.298 23.518 27.317 1.00 34.01	PROT
••	ATOM	1339 CZ TYR 395	30.014 23.322 25.979 1.00 33.73 28.824 23.785 25.453 1.00 44.99	PROT
30	ATOM	1340 OH TYR 395		PROT
	ATOM	1341 C TYR 395	35.208 21.490 29.584 1.00 19.03 35.003 20.494 30.277 1.00 25.23	PROT
	ATOM	1342 O TYR 395		PROT
	ATOM	1343 N GLN 396	36.437 21.883 29.256 1.00 17.76 37.596 21.134 29.725 1.00 13.73	PROT
26	ATOM	1344 CA GLN 396 1345 CB GLN 396	37.396 21.134 29.723 1.00 13.73 38.905 21.766 29.240 1.00 2.45	PROT
35	ATOM		40.061 20.767 29.110 1.00 2.00	PROT
	ATOM	1346 CG GLN 396	41.388 21.439 28.799 1.00 5.12	PROT
	ATOM	1347 CD GLN 396	41.706 22.484 29.359 1.00 10.11	PROT
		1348 OE1 GLN 396	42.169 20.840 27.903 1.00 9.09	PROT
40		1349 NE2 GLN 396	37.562 21.149 31.238 1.00 17.65	PROT
40		1350 C GLN 396		PROT
		1351 O GLN 396	37.802 20.125 31.894 1.00 9.63	PROT
		1352 N ASP 397	37.250 22.319 31.787 1.00 6.69	
		1353 CA ASP 397	37.178 22.476 33.226 1.00 9.36 36.732 23.893 33.570 1.00 11.44	PROT PROT
45		1355 CG ASP 397	37.867 24.891 33.446 1.00 18.32	PROT PROT
		1356 OD1 ASP 397	39.033 24.438 33.397 1.00 24.00 37.615 26.114 33.395 1.00 20.67	PROT
		1357 OD2 ASP 397	36.215 21.443 33.771 1.00 7.77	PROT
		1358 C ASP 397	36.497 20.771 34.761 1.00 7.77	PROT
50		1359 O ASP 397	35.087 21.293 33.093 1.00 9.19	PROT
50	ATOM	1360 N SER 398	33.067 21.293 33.093 1.00 9.19	rkui

	ATOM	1361 CA SER 398	34.094 20.322 33.508 1.00 14.18	PROT
	ATOM	1362 CB SER 398	32.916 20.334 32.542 1.00 12.11	PROT
	ATOM	1363 OG SER 398	32.406 21.650 32.423 1.00 31.95	PROT
	ATOM	1364 C SER 398	34.712 18.939 33.556 1.00 11.47	PROT
5	ATOM	1365 O SER 398	34.591 18.227 34.551 1.00 21.11	PROT
	ATOM	1366 N PHE 399	35.394 18.565 32.485 1.00 18.68	PROT
	ATOM	1367 CA PHE 399	36.017 17.252 32.417 1.00 24.93	PROT
	ATOM	1368 CB PHE 399	36.587 17.012 31.014 1.00 23.38	PROT
	ATOM	1369 CG PHE 399	35.543 16.705 29.981 1.00 20.19	PROT
10	ATOM	1370 CD1 PHE 399	35.224 17.638 28.997 1.00 22.94	PROT
	ATOM	1371 CD2 PHE 399	34.878 15.486 29.988 1.00 8.62	PROT
	ATOM	1372 CE1 PHE 399	34.257 17.361 28.029 1.00 12.53	PROT
	ATOM	1373 CE2 PHE 399	33.914 15.201 29.027 1.00 19.25	PROT
	ATOM	1374 CZ PHE 399	33.604 16.143 28.044 1.00 15.15	PROT
15	ATOM	1375 C PHE 399	37.113 17.097 33.463 1.00 23.06	PROT
	ATOM	1376 O PHE 399	37.210 16.063 34.137 1.00 15.58	PROT
	ATOM	1377 N LEU 400	37.932 18.131 33.604 1.00 22.12	PROT
	ATOM	1378 CA LEU 400	39.017 18.095 34.567 1.00 18.27	PROT
	ATOM	1379 CB LEU 400	39.846 19.372 34.461 1.00 10.06	PROT
20	ATOM	1380 CG LEU 400	41.021 19.248 33.491 1.00 8.13	PROT
	ATOM	1381 CD1 LEU 400	41.616 20.594 33.195 1.00 2.00	PROT
	ATOM	1382 CD2 LEU 400	42.055 18.333 34.095 1.00 13.73	PROT
	ATOM	1383 C LEU 400	38.527 17.892 36.002 1.00 24.79	PROT
	ATOM	1384 O LEU 400	39.189 17.228 36.787 1.00 26.46	PROT
25	ATOM	1385 N LEU 401	37.371 18.447 36.354 1.00 21.93	PROT
	ATOM	1386 CA LEU 401	36.862 18.268 37.707 1.00 17.21	PROT
	ATOM	1387 CB LEU 401	35.766 19.285 38.022 1.00 19.27	PROT
	ATOM	1388 CG LEU 401	35.538 19.547 39.515 1.00 16.76	PROT
	ATOM	1389 CD1 LEU 401	36.652 20.403 40.085 1.00 2.00	PROT
30	ATOM	1390 CD2 LEU 401	34.206 20.235 39.687 1.00 14.41	PROT
	ATOM	1391 C LEU 401	36.316 16.864 37.879 1.00 18.03	PROT
	ATOM	1392 O LEU 401	36.482 16.250 38.925 1.00 28.63	PROT
	ATOM	1393 N ALA 402	35.656 16.346 36.856 1.00 9.30	PROT
	ATOM	1394 CA ALA 402	35.124 15.000 36.951 1.00 7.03	PROT
35	ATOM	1395 CB ALA 402	34.233 14.703 35.758 1.00 14.15	PROT
	ATOM	1396 C ALA 402	36.298 14.029 36.989 1.00 7.68	PROT
	ATOM	1397 O ALA 402	36.294 13.054 37.739 1.00 2.00	PROT
	ATOM	1398 N PHE 403	37.311 14.305 36.178 1.00 4.49	PROT
40	ATOM	1399 CA PHE 403	38.477 13.439 36.140 1.00 9.18	PROT
40	ATOM	1400 CB PHE 403	39.510 13.977 35.138 1.00 12.80	PROT
	ATOM	1401 CG PHE 403	40.545 12.957 34.693 1.00 5.42	PROT
	ATOM	1402 CD1 PHE 403	41.590 13.334 33.859 1.00 2.00	PROT
	ATOM	1403 CD2 PHE 403	40.480 11.634 35.103 1.00 2.00	PROT
4.5	ATOM	1404 CE1 PHE 403	42.546 12.410 33.448 1.00 2.00	PROT
45	ATOM	1405 CE2 PHE 403	41.440 10.711 34.688 1.00 2.00	PROT
	ATOM	1406 CZ PHE 403	42.468 11.100 33.863 1.00 2.00 39.080 13.366 37.539 1.00 10.08	PROT PROT
	ATOM	1407 C PHE 403	39.080 13.366 37.539 1.00 10.08 39.207 12.279 38.097 1.00 8.23	PROT
	ATOM	1408 O PHE 403 1409 N GLU 404	39.207 12.279 38.097 1.00 8.23 39.451 14.514 38.103 1.00 12.64	PROT
50	ATOM ATOM	1410 CA GLU 404	40.030 14.546 39.448 1.00 19.23	PROT
50	ATOM	1410 CA GLU 404	40.030 14.370 37.470 1.00 17.23	1101

	ATOM	1411 CB GLU 404 40.227 15.989 39.942 1.00 19.80 PROT	•
	ATOM	1412 CG GLU 404 41.532 16.220 40.728 1.00 24.03 PROT	•
	ATOM	1413 CD GLU 404 41.474 17.429 41.655 1.00 29.60 PROT	•
	ATOM	1414 OE1 GLU 404 41.706 18.565 41.182 1.00 29.51 PRO	Γ
5	ATOM	1415 OE2 GLU 404 41.197 17.247 42.861 1.00 30.42 PRO	Γ
-	ATOM	1416 C GLU 404 39.112 13.806 40.416 1.00 24.36 PROT	
	ATOM	1417 O GLU 404 39.571 12.963 41.200 1.00 28.04 PROT	
	ATOM	1418 N HIS 405 37.815 14.108 40.358 1.00 10.26 PROT	
	ATOM	1419 CA HIS 405 36.870 13.446 41.240 1.00 7.78 PROT	
10	ATOM	1420 CB HIS 405 35.473 14.023 41.054 1.00 3.47 PROT	
	ATOM	1421 CG HIS 405 35.312 15.393 41.630 1.00 15.49 PROT	
	ATOM	1422 CD2 HIS 405 36.223 16.260 42.134 1.00 17.97 PROT	
	ATOM	1423 ND1 HIS 405 34.096 16:036 41.694 1.00 21.57 PROT	
	ATOM	1424 CE1 HIS 405 34.265 17.242 42.210 1.00 27.50 PROT	
15	ATOM	1425 NE2 HIS 405 35.547 17.403 42.485 1.00 13.53 PROT	
	ATOM	1426 C HIS 405 36.856 11.936 41.005 1.00 14.88 PROT	
	ATOM	1427 O HIS 405 36.641 11.155 41.935 1.00 22.11 PROT	
	ATOM	1428 N TYR 406 37.091 11.512 39.767 1.00 16.52 PROT	
	ATOM	1429 CA TYR 406 37.085 10.083 39.491 1.00 14.35 PROT	•
20	ATOM	1430 CB TYR 406 37.007 9.808 37.989 1.00 9.90 PROT	
	ATOM	1431 CG TYR 406 36.840 8.346 37.657 1.00 2.00 PROT	
	ATOM	1432 CD1 TYR 406 35.587 7.742 37.676 1.00 8.84 PROT	
	ATOM	1433 CE1 TYR 406 35.433 6.382 37.386 1.00 8.78 PROT	_
	ATOM	1434 CD2 TYR 406 37.939 7.562 37.338 1.00 15.34 PROT	
25	ATOM	1435 CE2 TYR 406 37.801 6.204 37.044 1.00 13.48 PROT	
	ATOM	1436 CZ TYR 406 36.548 5.624 37.073 1.00 15.64 PROT	
	ATOM	1437 OH TYR 406 36.431 4.287 36.804 1.00 2.00 PROT	
	ATOM	1438 C TYR 406 38.340 9.466 40.071 1.00 9.54 PROT	
	ATOM	1439 O TYR 406 38.328 8.328 40.525 1.00 14.29 PROT	
30	ATOM	1440 N ILE 407 39.430 10.217 40.058 1.00 6.56 PROT	
	ATOM	1441 CA ILE 407 40.671 9.708 40.617 1.00 13.87 PROT	
	ATOM	1442 CB ILE 407 41.808 10.728 40.474 1.00 11.28 PROT 1443 CG2 ILE 407 42.902 10.413 41.461 1.00 6.25 PROT	
	ATOM	1115 002 122 101	
	ATOM	1441 661 122 101	
35	ATOM	*	
	ATOM	1410 6 122 101	
	ATOM	• • • • • • • • • • • • • • • • • • • •	
	ATOM	1448 N ASN 408 39.953 10.448 42.792 1.00 12.35 PROT 1449 CA ASN 408 39.642 10.363 44.213 1.00 2.00 PROT	
40	ATOM	1450 CB ASN 408 38.758 11.535 44.629 1.00 2.00 PROT	
40	ATOM	1451 CG ASN 408 39.499 12.840 44.657 1.00 3.57 PROT	
	ATOM ATOM	1451 CG ASN 408 39.499 12.850 44.656 1.00 14.35 PRO	
	ATOM	1453 ND2 ASN 408 38.758 13.949 44.689 1.00 2.00 PRO	
	ATOM	1454 C ASN 408 38.868 9.078 44.432 1.00 6.49 PROT	•
15	ATOM	1455 O ASN 408 39.282 8.187 45.178 1.00 10.45 PROT	
45	ATOM	1456 N TYR 409 37.731 8.987 43.766 1.00 2.00 PROT	
	ATOM	1457 CA TYR 409 36.900 7.816 43.893 1.00 9.20 PROT	
	ATOM		
	ATOM	1459 CG TYR 409 35.121 6.489 42.683 1.00 12.54 PROT	
50	ATOM	1460 CD1 TYR 409 33.984 6.281 43.456 1.00 29.23 PRO	
50	A I OIVI	1700 CD1 111C 707 35.701 0.201 151100 1100 27125 11CO.	-

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33.285 5.077 43.403 1.00 25.45
                                                             PROT
    ATOM 1461 CE1 TYR 409
    ATOM 1462 CD2 TYR 409
                                35.547 5.465 41.850 1.00 24.96
                                                             PROT
                               34.860 4.259 41.788 1.00 33.40
                                                             PROT
    ATOM 1463 CE2 TYR 409
                               33.733 4.074 42.567 1.00 24.27
                                                             PROT
    ATOM 1464 CZ TYR 409
                               33.065 2.883 42.509 1.00 32.72
                                                             PROT
    ATOM 1465 OH TYR 409
    ATOM 1466 C TYR 409
                              37.753 6.553 43.867 1.00 13.96
                                                            PROT
                              37.730 5.763 44.804 1.00 29.48
                                                            PROT
    ATOM 1467 O TYR 409
                               38.531 6.399 42.803 1.00 23.04
                                                             PROT
    ATOM 1468 N ARG 410
                               39.377 5.230 42.588 1.00 22.09
    ATOM 1469 CA ARG 410
                                                             PROT
                               39.982 5.327 41.190 1.00 13.24
                                                             PROT
    ATOM 1470 CB ARG 410
10
                               38.947 5.399 40.090 1.00 14.01
                                                             PROT
    ATOM 1471 CG ARG 410
                               38.934 4.111 39.275 1.00 16.49
                                                             PROT
    ATOM 1472 CD ARG 410
                               40,227 3.848 38.651 1.00 9.77
                                                             PROT
    ATOM 1473 NE ARG 410
                               40.617 2.651 38.239 1.00 11.38
                                                             PROT
    ATOM 1474 CZ ARG 410
                                41.806 2.493 37.685 1.00 14.94
    ATOM 1475 NH1 ARG 410
                                                              PROT
15
                                39.810 1.613 38.375 1.00 12.78
                                                              PROT
    ATOM 1476 NH2 ARG 410
                               40.486 4.914 43.604 1.00 24.49
    ATOM 1477 C ARG 410
                                                            PROT
                               40.860 3.753 43.780 1.00 12.85
    ATOM 1478 O ARG 410
                                                            PROT
                              41.023 5.931 44.262 1.00 24.16
                                                            PROT
    ATOM 1479 N LYS 411
                               42.085 5.706 45.235 1.00 27.14
                                                             PROT
    ATOM 1480 CA LYS 411
20
                               41.525 5.069 46.516 1.00 37.40
    ATOM 1481 CB LYS 411
                                                             PROT
                               40.317 5.779 47.103 1.00 35.00
                                                             PROT
    ATOM 1482 CG LYS 411
    ATOM 1483 CD LYS 411
                               39.406 4.788 47.804 1.00 40.83
                                                             PROT
                               38.414 5.496 48.725 1.00 58.04
                                                             PROT
    ATOM 1484 CE LYS 411
                               38.833 5.496 50.168 1.00 54.40
                                                             PROT
    ATOM 1485 NZ LYS 411
25
                                                            PROT
                              43.186 4.814 44.664 1.00 28.02
    ATOM 1486 C LYS 411
                                                            PROT
    ATOM 1487 O LYS 411
                              43.209 3.598 44.876 1.00 25.00
                              44.091 5.438 43.923 1.00 30.05
                                                            PROT
    ATOM 1488 N HIS 412
                               45.223 4.738 43.332 1.00 26.70
                                                            PROT
    ATOM 1489 CA HIS 412
                              45.756 5.491 42.104 1.00 29.28
                                                            PROT
    ATOM 1490 CB HIS 412
30
                                                            PROT
                               44.953 5.289 40.857 1.00 18.44
    ATOM 1491 CG HIS 412
     ATOM 1492 CD2 HIS 412
                               43.783 5.836 40.451 1.00 19.98
                                                             PROT
                                                             PROT
     ATOM 1493 ND1 HIS 412
                               45.366 4.465 39.833 1.00 16.33
                               44.486 4.513 38.850 1.00 24.80
                                                             PROT
     ATOM 1494 CE1 HIS 412
                               43.516 5.338 39.200 1.00 23.01
                                                             PROT
     ATOM 1495 NE2 HIS 412
35
                              46.281 4.788 44.406 1.00 20.73
                                                           PROT
     ATOM 1496 C HIS 412
                              46,335 5.740 45.171 1.00 24.69
                                                            PROT
     ATOM 1497 O HIS 412
                                                            PROT
                              47.138 3.784 44.461 1.00 28.17
     ATOM 1498 N HIS 413
                               48.183 3.788 45.465 1.00 28.09
                                                            PROT
     ATOM 1499 CA HIS 413
                                                            PROT
                               48.219 2.426 46.144 1.00 21.71
40
     ATOM 1500 CB HIS 413
     ATOM 1501 CG HIS 413
                               46.906 2.053 46.759 1.00 44.26
                                                             PROT
                               46.140 0.941 46.632 1.00 43.48
                                                             PROT
     ATOM 1502 CD2 HIS 413
     ATOM 1503 ND1 HIS 413
                               46.214 2.902 47.600 1.00 40.00
                                                             PROT
                                                             PROT
                               45.080 2.328 47.962 1.00 47.35
     ATOM 1504 CE1 HIS 413
                               45.011 1.137 47.390 1.00 35.50
                                                             PROT
     ATOM 1505 NE2 HIS 413
45
                              49.527 4.194 44.875 1.00 26.49
                                                            PROT
     ATOM 1506 C HIS 413
                              50.483 3.421 44.829 1.00 31.82
                                                            PROT
     ATOM 1507 O HIS 413
                               49.555 5.439 44.411 1.00 18.32
                                                             PROT
     ATOM 1508 N VAL 414
                                                             PROT
     ATOM 1509 CA VAL 414
                                50.726 6.069 43.820 1.00 22.60
                                50.718 5.966 42.290 1.00 32.50
                                                             PROT
     ATOM 1510 CB VAL 414
50
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	ATOM	1511 CG1 VAL 414 51.636 7.026 41.694 1.00 33.83	PROT
	ATOM	1512 CG2 VAL 414 51.169 4.574 41.863 1.00 40.20	PROT
	ATOM	1513 C VAL 414 50.630 7.529 44.225 1.00 17.96	PROT
	ATOM	1514 O VAL 414 49.708 8.236 43.829 1.00 30.33	PROT
5	ATOM	1515 N THR 415 51.586 7.969 45.028 1.00 32.51	PROT
	ATOM	1516 CA THR 415 51.601 9.332 45.531 1.00 35.31	PROT
	ATOM	1517 CB THR 415 52.779 9.529 46.511 1.00 49.75	PROT
	ATOM	1518 OG1 THR 415 53.023 10.930 46.702 1.00 60.64	PROT
	ATOM	1519 CG2 THR 415 54.038 8.850 45.974 1.00 50.83	PROT
10	ATOM	1520 C THR 415 51.668 10.387 44.436 1.00 31.44	PROT.
	ATOM	1521 O THR 415 52.423 10.251 43.475 1.00 22.01	PROT
	ATOM	1522 N HIS 416 50.865 11.437 44.607 1.00 24.94	PROT
	ATOM	1523 CA HIS 416 50.781 12.559 43.671 1.00 27.82	PROT
•	ATOM	1524 CB HIS 416 52.163 13.164 43.440 1.00 32.98	PROT
15	ATOM	1525 CG HIS 416 52.776 13.747 44.671 1.00 44.74	PROT
	ATOM	1526 CD2 HIS 416 53.982 13.539 45.251 1.00 44.91	PROT
	ATOM	1527 ND1 HIS 416 52.121 14.665 45.462 1.00 49.20	PROT
	ATOM	1528 CE1 HIS 416 52.899 15.000 46.477 1.00 53.14	PROT
	ATOM	1529 NE2 HIS 416 54.033 14.330 46.373 1.00 41.72	PROT
20	ATOM	1530 C HIS 416 50.176 12.172 42.328 1.00 29.13	PROT
	ATOM	1531 O HIS 416 50.612 12.660 41.286 1.00 37.24	PROT
	ATOM	1532 N PHE 417 49.163 11.311 42.350 1.00 18.38	PROT
	ATOM	1533 CA PHE 417 48.528 10.867 41.115 1.00 16.08	PROT
	ATOM	1534 CB PHE 417 47.295 10.029 41.407 1.00 17.89	PROT
25	ATOM	1535 CG PHE 417 47.021 8.997 40.364 1.00 16.15	PROT
		1536 CD1 PHE 417 47.980 8.044 40.051 1.00 16.55	PROT
	ATOM	1537 CD2 PHE 417 45.806 8.971 39.696 1.00 15.49	PROT
		1538 CE1 PHE 417 47.727 7.081 39.087 1.00 19.81	PROT
		1539 CE2 PHE 417 45.544 8.008 38.731 1.00 9.76	PROT
30	ATOM	1540 CZ PHE 417 46.501 7.064 38.427 1.00 5.25	PROT
	ATOM	1541 C PHE 417 48.117 11.990 40.187 1.00 14.51	PROT
	ATOM	1542 O PHE 417 48.636 12.119 39.081 1.00 18.44	PROT
	ATOM	1543 N TRP 418 47.171 12.800 40.640 1.00 21.08	PROT
	ATOM	1544 CA TRP 418 46.688 13.900 39.828 1.00 16.28	PROT
35	ATOM	1545 CB TRP 418 45.796 14.832 40.659 1.00 15.19	PROT
	ATOM	1546 CG TRP 418 45.002 15.746 39.802 1.00 16.60	PROT
	ATOM	1547 CD2 TRP 418 44.165 15.369 38.710 1.00 21.85	PROT
	ATOM	1548 CE2 TRP 418 43.690 16.557 38.118 1.00 22.53	PROT
4.0	ATOM	1549 CE3 TRP 418 43.771 14.138 38.170 1.00 16.42	PROT
40	ATOM	1550 CD1 TRP 418 44.999 17.107 39.836 1.00 21.01	PROT
	ATOM	1551 NEI TRP 418 44.215 17.606 38.826 1.00 24.02	PROT
	ATOM	1552 CZ2 TRP 418 42.838 16.555 37.010 1.00 24.64	PROT
	ATOM	1553 CZ3 TRP 418 42.925 14.135 37.069 1.00 28.80	PROT
4.0	ATOM	1554 CH2 TRP 418 42.467 15.337 36.500 1.00 21.25	PROT PROT
45	ATOM	1555 C TRP 418 47.834 14.676 39.192 1.00 16.17	
	ATOM	1556 O TRP 418 47.928 14.764 37.977 1.00 19.51	PROT PROT
	ATOM	1557 N PRO 419 48.723 15.250 40.007 1.00 19.59	PROT
	ATOM	1558 CD PRO 419 48.757 15.274 41.477 1.00 19.81	PROT
50	ATOM	1559 CA PRO 419 49.837 16.002 39.429 1.00 17.87 1560 CB PRO 419 50.720 16.309 40.629 1.00 6.85	
50	ATOM	1560 CB PRO 419 50.720 16.309 40.629 1.00 6.85	PROT

	ATOM	1561 CG PRO 419	49.785 16.326 41.764 1.00 25.11	PROT
	ATOM	1562 C PRO 419	50.578 15.202 38.373 1.00 15.44	PROT
	ATOM	1563 O PRO 419	50.922 15.720 37.315 1.00 24.75	PROT
	ATOM	1564 N LYS 420	50.811 13.932 38.664 1.00 15.10	PROT
5	ATOM	1565 CA LYS 420	51.534 13.056 37.748 1.00 20.59	PROT
•	ATOM	1566 CB LYS 420	51.900 11.746 38.471 1.00 28.85	PROT
	ATOM	1567 CG LYS 420	52.955 11.906 39.577 1.00 30.61	PROT
	ATOM	1568 CD LYS 420	52.907 10.759 40.580 1.00 24.41	PROT
	ATOM	1569 CE LYS 420	54.275 10.493 41.224 1.00 31.94	PROT
10	ATOM	1570 NZ LYS 420	54.485 9.040 41.557 1.00 27.34	PROT
	ATOM	1571 C LYS 420	50.779 12.757 36.445 1.00 17.36	PROT
	ATOM	1572 O LYS 420	51.393 12.439 35.437 1.00 26.28	PROT
	ATOM	1573 N LEU 421	49.455 12.859 36.474 1.00 16.34	PROT
	ATOM	1574 CA LEU 421	48.627 12.614 35.297 1.00 9.38	PROT
15	ATOM	1575 CB LEU 421	47.231 12.139 35.707 1.00 13.22	, PROT
	ATOM	1576 CG LEU 421	46.739 10.818 35.107 1.00 15.75	PROT
	ATOM	1577 CD1 LEU 421	47.919 9.993 34.652 1.00 29.24	PROT
	ATOM	1578 CD2 LEU 421	45.949 10.049 36.135 1.00 12.19	PROT
	ATOM	1579 C LEU 421	48.511 13.866 34.441 1.00 12.61	PROT
20	ATOM	1580 O LEU 421	48.458 13.777 33.223 1.00 17.85	PROT
	ATOM	1581 N LEU 422	48.451 15.036 35.063 1.00 8.47	PROT
	ATOM	1582 CA LEU 422	48.393 16.254 34.277 1.00 7.21	PROT
	ATOM	1583 CB LEU 422	48.160 17.468 35.164 1.00 2.00	PROT
	ATOM	1584 CG LEU 422	46.941 17.445 36.088 1.00 12.16	PROT
25	ATOM	1585 CD1 LEU 422	47.024 18.660 36.982 1.00 6.96	PROT
	ATOM	1586 CD2 LEU 422	45.632 17.450 35.313 1.00 2.00	PROT
	ATOM	1587 C LEU 422	49.748 16.365 33.567 1.00 10.59	PROT
	ATOM	1588 O LEU 422	49.851 16.938 32.477 1.00 13.48	PROT
	ATOM	1589 N MET 423	50.786 15.804 34.185 1.00 2.29	PROT
30	ATOM	1590 CA MET 423	52.109 15.821 33.579 1.00 6.50	PROT
	ATOM	1591 CB MET 423	53.158 15.215 34.514 1.00 2.13	PROT
	ATOM	1592 CG MET 423	53.361 15.968 35.803 1.00 16.33	PROT
	ATOM	1593 SD MET 423	55.075 16.415 36.070 1.00 26.66	PROT
	ATOM	1594 CE MET 423	55.751 14.880 36.623 1.00 20.24	PROT
35	ATOM	1595 C MET 423	52.016 14.966 32.318 1.00 12.20	PROT
	ATOM	1596 O MET 423	52.741 15.183 31.345 1.00 18.67	PROT
	ATOM	1597 N LYS 424	51.114 13.988 32.352 1.00 7.89	PROT
	ATOM	1598 CA LYS 424	50.907 13.084 31.230 1.00 12.91	PROT
	ATOM	1599 CB LYS 424	49.990 11.924 31.645 1.00 5.14	PROT
40	ATOM	1600 CG LYS 424	50.669 10.579 31.980 1.00 11.76	PROT
	ATOM	1601 CD LYS 424	52.187 10.590 31.866 1.00 3.70	PROT
	ATOM	1602 CE LYS 424	52.844 10.020 33.113 1.00 7.84	PROT
	ATOM	1603 NZ LYS 424	54.335 9.959 32.995 1.00 25.86	PROT
	ATOM	1604 C LYS 424	50.293 13.840 30.046 1.00 17.44	PROT
45	ATOM	1605 O LYS 424	50.650 13.596 28.897 1.00 11.72	PROT
	ATOM	1606 N VAL 425	49.370 14.756 30.322 1.00 3.16	PROT
	ATOM	1607 CA VAL 425	48.768 15.515 29.249 1.00 2.00	PROT
	ATOM	_	47.744 16.532 29.773 1.00 6.77	PROT
	ATOM			PROT
50	ATOM	1610 CG2 VAL 425	46.381 15.870 29.914 1.00 10.91	PROT

	ATOM	1611 C VAL 425	49.845 16.274 28.487 1.00 4.83	PROT
	ATOM	1612 O VAL 425	49.853 16.265 27.269 1.00 15.69	PROT
	ATOM	1613 N THR 426	50.753 16.924 29.208 1.00 14.38	PROT
	ATOM	1614 CA THR 426	51.824 17.707 28.593 1.00 12.41	PROT
5	ATOM	1615 CB THR 426	52.713 18.372 29.667 1.00 12.49	PROT
	ATOM	1616 OG1 THR 426	51.890 19.138 30.552 1.00 11.06	PROT
	ATOM	1617 CG2 THR 426	53.763 19.283 29.015 1.00 2.93	PROT
	ATOM	1618 C THR 426	52.734 16.928 27.653 1.00 15.72	PROT
	ATOM	1619 O THR 426	53.198 17.463 26.651 1.00 14.40	PROT
10	ATOM	1620 N ASP 427	53.000 15.672 27.981 1.00 16.23	PROT
••	ATOM	1621 CA ASP 427	53.865 14.843 27.157 1.00 16.35	PROT
	ATOM	1622 CB ASP 427	54.342 13.630 27.950 1.00 19.48	PROT
	ATOM	1623 CG ASP 427	55.337 13.997 29.029 1.00 18.96	PROT
	ATOM	1624 OD1 ASP 427	55.874 15.125 29.010 1.00 8.75	PROT
15	ATOM	1625 OD2 ASP 427	55.579 13.145 29.902 1.00 24.25	PROT
	ATOM	1626 C ASP 427	53.155 14.381 25.891 1.00 20.52	PROT
	ATOM	1627 O ASP 427	53.793 14.164 24.856 1.00 25.69	PROT
	ATOM	1628 N LEU 428	51.838 14.218 25.986 1.00 5.49	PROT
	ATOM	1629 CA LEU 428	51.040 13.815 24.849 1.00 2.00	PROT
20	ATOM	1630 CB LEU 428	49.634 13.470 25.301 1.00 2.00	PROT
	ATOM	1631 CG LEU 428	49.579 12.127 26.028 1.00 2.00	PROT
•	ATOM	1632 CD1 LEU 428	48.184 11.789 26.481 1.00 2.00	PROT
	ATOM	1633 CD2 LEU 428	50.088 11.080 25.108 1.00 2.00	PROT
	ATOM	1634 C LEU 428	51.019 14.987 23.881 1.00 7.72	PROT
25	ATOM-	1635 O LEU 428	51.072 14.800 22.666 1.00 9.22	PROT
	ATOM	1636 N ARG 429	50.961 16.197 24.432 1.00 10.07	PROT
	ATOM	1637 CA ARG 429	50.948 17.438 23.659 1.00 7.97	PROT
	ATOM	1638 CB ARG 429	50.799 18.642 24.583 1.00 18.55	PROT
•	ATOM	1639 CG ARG 429	49.548 18.634 25.429 1.00 14.80	PROT
30	ATOM	1640 CD ARG 429	48.588 19.674 24.935 1.00 32.08	PROT
	ATOM	1641 NE ARG 429	47.508 19.923 25.880 1.00 42.46	PROT
	ATOM	1642 CZ ARG 429	46.226 19.673 25.631 1.00 48.51	PROT
	ATOM	1643 NH1 ARG 429	45.860 19.163 24.459 1.00 33.35	PROT
	ATOM	1644 NH2 ARG 429		PROT
35	ATOM	1645 C ARG 429	52.260 17.557 22.919 1.00 11.77	PROT
	ATOM	1646 O ARG 429	52.298 17.904 21.737 1.00 28.66	PROT
	ATOM	1647 N MET 430	53.343 17.270 23.629 1.00 20.26	PROT
		1648 CA MET 430	54.671 17.328 23.042 1.00 21.06	PROT
	ATOM	1649 CB MET 430	55.738 17.015 24.100 1.00 30.24	PROT
40	ATOM	1650 CG MET 430	56.061 18.165 25.056 1.00 34.66	PROT
	ATOM	1651 SD MET 430	55.727 19.795 24.373 1.00 35.91	PROT
	ATOM	1652 CE MET 430	56.839 19.814 22.978 1.00 32.52	PROT
	ATOM	1653 C MET 430	54.735 16.302 21.925 1.00 18.70	PROT
	ATOM	1654 O MET 430	55.287 16.560 20.860 1.00 16.59	PROT
45	ATOM	1655 N ILE 431	54.161 15.133 22.182 1.00 15.38	PROT
	ATOM	1656 CA ILE 431	54.144 14.069 21.196 1.00 15.85	PROT
	ATOM	1657 CB ILE 431	53.326 12.859 21.705 1.00 13.76	PROT
	ATOM	1658 CG2 ILE 431	52.727 12.084 20.539 1.00 11.11	PROT
~ ^	ATOM	1659 CG1 ILE 431	54.239 11.924 22.489 1.00 11.72	PROT PROT
50	ATOM	1660 CD1 ILE 431	53.552 11.224 23.615 1.00 16.22	LVOI

	ATOM	1661 C ILE 431 53.538 14.609 19.904 1.00 18.49 PROT
	ATOM	1662 O ILE 431 54.134 14.483 18.839 1.00 17.36 PROT
	ATOM	1663 N GLY 432 52.361 15.220 20.003 1.00 2.00 PROT
	ATOM	1664 CA GLY 432 51.721 15.772 18.831 1.00 2.00 PROT
5	ATOM	1665 C GLY 432 52.542 16.851 18.148 1.00 10.55 PROT
-	ATOM	1666 O GLY 432 52.707 16.834 16.936 1.00 9.60 PROT
	ATOM	1667 N ALA 433 53.043 17.805 18.926 1.00 11.17 PROT
	ATOM	1668 CA ALA 433 53.855 18.884 18.385 1.00 2.00 PROT
	ATOM	1669 CB ALA 433 54.326 19.771 19.506 1.00 2.00 PROT
10	ATOM	1670 C ALA 433 55.050 18.285 17.646 1.00 6.43 PROT
	ATOM	1671 O ALA 433 55.493 18.789 16.623 1.00 11.71 PROT
	ATOM	1672 N CYS 434 55.579 17.197 18.179 1.00 15.71 PROT
	ATOM	1673 CA CYS 434 56.715 16.534 17.573 1.00 13.44 PROT
	ATOM	1674 CB CYS 434 57.228 15.464 18.518 1.00 14.76 PROT
15	ATOM	1675 SG CYS 434 58.910 15.703 18.985 1.00 20.82 PROT
	ATOM	1676 C CYS 434 56.269 15.902 16.264 1.00 9.28 PROT
	ATOM	1677 O CYS 434 56.969 15.948 15.256 1.00 8.50 PROT
	ATOM	1678 N HIS 435 55.091 15.300 16.298 1.00 11.04 PROT
	ATOM	1679 CA HIS 435 54.533 14.657 15.122 1.00 11.30 PROT
20	ATOM	1680 CB HIS 435 53.142 14.132 15.438 1.00 4.30 PROT
	ATOM	1681 CG HIS 435 52.480 13.460 14.283 1.00 13.68 PROT
	ATOM	1682 CD2 HIS 435 52.751 12.288 13.662 1.00 4.72 PROT
	ATOM	1683 ND1 HIS 435 51.358 13.976 13.666 1.00 5.53 PROT
	ATOM	1684 CE1 HIS 435 50.966 13.147 12.717 1.00 12.84 PROT
25	ATOM	1685 NE2 HIS 435 51.794 12.116 12.694 1.00 15.77 PROT
	ATOM	1686 C HIS 435 54.482 15.661 13.973 1.00 8.50 PROT
	ATOM	1687 O HIS 435 54.941 15.370 12.869 1.00 14.82 PROT
	ATOM	1688 N ALA 436 53.938 16.844 14.245 1.00 5.74 PROT
	ATOM	1689 CA ALA 436 53.843 17.905 13.252 1.00 2.00 PROT
30	ATOM	1690 CB ALA 436 53.632 19.241 13.942 1.00 2.00 PROT
	ATOM	1691 C ALA 436 55.121 17.934 12.406 1.00 8.68 PROT
	ATOM	1692 O ALA 436 55.080 17.712 11.193 1.00 15.14 PROT
	ATOM	1693 N SER 437 56.256 18.189 13.047 1.00 6.82 PROT 1694 CA SER 437 57 522 18.226 12.337 1.00 9.05 PROT
	ATOM	TOY OIL BER 157 STREET TOTAL
35	ATOM	1075 CB BER 137 COIGHT STATE
	ATOM	
	ATOM	
	ATOM	
40	ATOM	1099 14 71100 130 371001 121002 121011
40	ATOM	1700 CA ARG 438 57.799 14.501 11.766 1.00 16.98 PROT 1701 CB ARG 438 57.294 13.409 12.702 1.00 24.77 PROT
	ATOM	1701 OB 1110 130
	ATOM	
	ATOM	
4.5	ATOM	1,0,1,0,1
45	ATOM	1705 CZ ARG 438 61.505 11.504 11.423 1.00 25.21 PROT 1706 NH1 ARG 438 62.077 10.641 10.603 1.00 39.58 PROT
	ATOM	THE THE STATE OF T
	ATOM ATOM	
	ATOM	7,00 0 1110 130 130 130 130 130 130 130 13
50	ATOM	10 101 1 00 1 CEC DDOT
JU	ATOM	1/10 14 FILE 35./01 14.075 10.101 1.00 10.10 1

		1711 CA PHE 439 54.933 14.878 9.303		PROT
	ATOM	1712 CB PHE 439 53.603 15.575 9.574		PROT
		1713 CG PHE 439 52.597 15.364 8.490		PROT
		1714 CD1 PHE 439 52.042 14.103 8.279		PROT
5		1715 CD2 PHE 439 52.265 16.394 7.622		PROT
		1716 CE1 PHE 439 51.175 13.867 7.206		PROT
		1717 CE2 PHE 439 51.404 16.173 6.552		PROT
		1718 CZ PHE 439 50.860 14.905 6.341		PROT
		1719 C PHE 439 55.620 15.548 8.130 1		PROT
10		1720 O PHE 439 55.512 15.095 6.987 1		PROT
		1721 N LEU 440 56.328 16.633 8.427 1		PROT
		1722 CA LEU 440 57.055 17.382 7.418		PROT
		1723 CB LEU 440 57.555 18.696 8.005		PROT
		1724 CG LEU 440 56.501 19.658 8.541		PROT
15		1725 CD1 LEU 440 57.152 20.985 8.855		PROT
		1726 CD2 LEU 440 55.410 19.847 7.522		PROT
		1727 C LEU 440 58.245 16.578 6.912 1		PROT
		1728 O LEU 440 58.506 16.526 5.718 1		PROT
		1729 N HIS 441 58.971 15.954 7.830 1.		PROT
20		1730 CA HIS 441 60.140 15.172 7.460 1		PROT
		1731 CB HIS 441 60.783 14.564 8.705 1		PROT
		1732 C HIS 441 59.724 14.081 6.497 1.		PROT
		1733 O HIS 441 60.461 13.725 5.579 1.		PROT
		1734 N MET 442 58.533 13.545 6.711		PROT
25		1735 CA MET 442 58.033 12.487 5.854		PROT
		1736 CB MET 442 56.871 11.776 6.551		PROT
		1737 CG MET 442 57.263 11.122 7.860		PROT
	ATOM	1738 SD MET 442 55.859 10.350 8.675		PROT
	ATOM	1739 CE MET 442 54.906 11.767 9.073		PROT
30	ATOM	1740 C MET 442 57.599 13.031 4.495		PROT
	ATOM	1741 O MET 442 57.887 12.431 3.461		PROT
	ATOM	1742 N LYS 443 56.920 14.175 4.503 1		PROT
	ATOM	1743 CA LYS 443 56.447 14.796 3.268		PROT
	ATOM	1744 CB LYS 443 55.767 16.129 3.574		PROT
35	ATOM	1745 CG LYS 443 54.303 15.989 3.953		PROT
	ATOM	1746 CD LYS 443 53.497 17.231 3.602		PROT
	ATOM	1747 CE LYS 443 52.204 16.848 2.861		PROT
	ATOM	1748 NZ LYS 443 50.931 17.261 3.564		PROT
	ATOM	1749 C LYS 443 57.570 15.007 2.251 1		PROT
40	ATOM	1750 O LYS 443 57.325 15.049 1.041 1		PROT
	ATOM	1751 N VAL 444 58.798 15.130 2.741		PROT
	ATOM	1752 CA VAL 444 59.942 15.318 1.867		PROT
	ATOM		1.00 29.15	PROT
	ATOM		1.00 29.48	PROT
45	ATOM		1.00 36.65	PROT
	ATOM	1756 C VAL 444 60.786 14.042 1.825		PROT
	ATOM	1757 O VAL 444 62.009 14.099 1.698		PROT
	ATOM	1758 N GLU 445 60.127 12.888 1.903		PROT
	ATOM	1759 CA GLU 445 60.842 11.612 1.896		PROT
50	ATOM	1760 CB GLU 445 61.429 11.360 3.282	1.00 50.55	PROT

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ATOM 1761 CG GLU 445
                                62.399 10.203 3.351 1.00 77.00
                                                             PROT
                               63.569 10.495 4.267 1.00 98.21
     ATOM 1762 CD GLU 445
                                                             PROT
     ATOM 1763 OE1 GLU 445
                                64.251 9.538 4.701 1.00100.00
                                                             PROT
    ATOM 1764 OE2 GLU 445
                                63.804 11.690 4.554 1.00100.00
                                                              PROT
    ATOM 1765 C GLU 445
                               59.989 10.408 1.491 1.00 43.41
                                                            PROT
                               60,466 9.274 1.511 1.00 48.80
     ATOM 1766 O GLU 445
                                                            PROT
                               58.731 10.644 1.137 1.00 38.17
     ATOM 1767 N CYS 446
                                                            PROT
     ATOM 1768 CA CYS 446
                               57.852 9.548 0.743 1.00 41.38
                                                            PROT
     ATOM 1769 CB CYS 446
                               57.066 9.035 1.965 1.00 40.61
                                                            PROT
     ATOM 1770 SG CYS 446
                               58.062 8.276 3.320 1.00 44.73
10
                                                            PROT
                               56.886 10.003 -0.362 1.00 45.83
    ATOM 1771 C CYS 446
                                                            PROT
    ATOM 1772 O CYS 446
                               56.466 11.184 -0.323 1.00 44.17
                                                            PROT
     ATOM 1773 OT CYS 446
                               56.570 9.180 -1.259 1.00 40.79
                                                            PROT
     ATOM 1774 CB GLU 449
                               52.635 12.140 -2.649 1.00 28.60
                                                             PROT
                               52.019 10.014 -1.526 1.00 38.06
    ATOM 1775 C GLU 449
                                                            PROT
15
     ATOM 1776 O GLU 449
                               50.873 10.220 -1.935 1.00 43.52
                                                            PROT
                               54.378 10.460 -2.167 1.00 17.78
     ATOM 1777 N GLU 449
                                                            PROT
     ATOM 1778 CA GLU 449
                               53.105 11.069 -1.689 1.00 33.80
                                                            PROT
     ATOM 1779 N LEU 450
                               52.387 8.880 -0.936 1.00 46.88
                                                            PROT
     ATOM 1780 CA LEU 450
                               51.432 7.808 -0.696 1.00 52.62
                                                            PROT
20
                               52.101 6.436 -0.850 1.00 57.50
     ATOM 1781 CB LEU 450
                                                            PROT
                               53.338 6.066 -0.028 1.00 59.81
     ATOM 1782 CG LEU 450
                                                            PROT
     ATOM 1783 CD1 LEU 450
                                53.613 4.573 -0.198 1.00 51.33
                                                             PROT
     ATOM 1784 CD2 LEU 450
                                54.544 6.890 -0.473 1.00 57.03
                                                             PROT
     ATOM 1785 C LEU 450
                              50.850 7.970 0.711 1.00 50.65
25
                                                           PROT
                               50.965 7.091 1.569 1.00 38.49
     ATOM 1786 O LEU 450
                                                            PROT
     ATOM 1787 N PHE 451
                               50.225 9.123 0.923 1.00 32.24
                                                            PROT:
     ATOM 1788 CA PHE 451
                               49.602 9.478 2.188 1.00 32.64
                                                            PROT
     ATOM 1789 CB PHE 451
                               50.091 10.857 2.648 1.00 56.06
                                                            PROT
     ATOM 1790 CG PHE 451
                               51.534 10.895 3.056 1.00 61.73
                                                             PROT
30
                                52.523 10.366 2.235 1.00 66.92
     ATOM 1791 CD1 PHE 451
                                                             PROT
                                51.905 11.486 4.256 1.00 58.76
     ATOM 1792 CD2 PHE 451
                                                             PROT
                               53.860 10.430 2.604 1.00 69.17
     ATOM 1793 CE1 PHE 451
                                                             PROT
                               53.231 11.556 4.635 1.00 61.48
     ATOM 1794 CE2 PHE 451
                                                             PROT
                               54.214 11.028 3.809 1.00 71.95
     ATOM 1795 CZ PHE 451
                                                            PROT
35
                              48.081 9.548 2.025 1.00 30.67
                                                           PROT
    ATOM 1796 C PHE 451
     ATOM 1797 O PHE 451
                               47.571 10.429 1.324 1.00 38.49
                                                            PROT
                               47.336 8.627 2.672 1.00 19.14
     ATOM 1798 N PRO 452
                                                            PROT
     ATOM 1799 CD PRO 452
                               47.774 7.495 3.510 1.00 24.21
                                                            PROT
     ATOM 1800 CA PRO 452
                               45.881 8.672 2.538 1.00 5.88
                                                            PROT
40
     ATOM 1801 CB PRO 452
                               45.397 7.742 3.633 1.00 16.92
                                                            PROT
                               46.496 6.737 3.761 1.00 16.91
     ATOM 1802 CG PRO 452
                                                            PROT
     ATOM 1803 C PRO 452
                               45,354 10.090 2.687 1.00 15.15
                                                            PROT
     ATOM 1804 O PRO 452
                               45.879 10.886 3.463 1.00 22.59
                                                            PROT
45
     ATOM 1805 N PRO 453
                               44.315 10.429 1.920 1.00 18.37
                                                            PROT
                               43.653 9.540 0.951 1.00 3.83
     ATOM 1806 CD PRO 453
                                                            PROT
     ATOM 1807 CA PRO 453
                               43.710 11.766 1.960 1.00 14.00
                                                             PROT
     ATOM 1808 CB PRO 453
                               42.502 11.649 1.032 1.00 20.04
                                                             PROT
                               42.316 10.163 0.807 1.00 19.43
     ATOM 1809 CG PRO 453
                                                             PROT
     ATOM 1810 C PRO 453
                              43.321 12.277 3.346 1.00 14.70
50
                                                            PROT
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	ATOM	1811 O PRO 453	43.609 13.422 3.682 1.00 9.70	PROT
	ATOM	1812 N LEU 454	42.667 11.446 4.152 1.00 25.39	PROT
	ATOM	1813 CA LEU 454	42.261 11.886 5.491 1.00 28.61	PROT
	ATOM	1814 CB LEU 454	41.463 10.804 6.217 1.00 17.29	PROT
5	ATOM	1815 CG LEU 454	40.893 11.224 7.572 1.00 9.05	PROT
-	ATOM	1816 CD1 LEU 454	40.174 12.547 7.435 1.00 17.23	PROT
	ATOM	1817 CD2 LEU 454	39.946 10.148 8.079 1.00 8.05	PROT
	ATOM	1818 C LEU 454	43.479 12.234 6.316 1.00 23.36	PROT
	ATOM	1819 O LEU 454	43.484 13.225 7.037 1.00 10.99	PROT
10	ATOM	1820 N PHE 455	44.503 11.394 6.205 1.00 14.26	PROT
	ATOM	1821 CA PHE 455	45.769 11.595 6.902 1.00 15.33	PROT
	ATOM	1822 CB PHE 455	46.761 10.496 6.501 1.00 26.32	PROT
	ATOM	1823 CG PHE 455	48.138 10.644 7.108 1.00 43.03	PROT
	ATOM	1824 CD1 PHE 455	48.305 11.094 8.414 1.00 43.52	PROT
15	ATOM	1825 CD2 PHE 455	49.270 10.282 6.380 1.00 41.44	PROT
13	ATOM	1826 CE1 PHE 455	49.576 11.176 8.987 1.00 37.77	PROT
	ATOM	1827 CE2 PHE 455	50.536 10.363 6.947 1.00 49.43	PROT
	ATOM	1828 CZ PHE 455	50.686 10.811 8.255 1.00 39.99	PROT
	ATOM	1829 C PHE 455	46.313 12.956 6.500 1.00 19.37	PROT
20	ATOM	1830 O PHE 455	46.945 13.646 7.298 1.00 29.31	PROT
20	ATOM	1831 N LEU 456	46.048 13.345 5.257 1.00 17.16	PROT
	ATOM	1832 CA LEU 456	46.527 14.625 4.750 1.00 20.15	PROT
	ATOM	1833 CB LEU 456	46.572 14.603 3.218 1.00 35.14	PROT
	ATOM	1834 CG LEU 456	47.593 13.660 2.568 1.00 40.45	PROT
25	ATOM	1835 CD1 LEU 456	47.233 13.456 1.116 1.00 44.38	PROT
23	ATOM	1836 CD2 LEU 456	48.990 14.234 2.680 1.00 34.88	PROT
	ATOM	1837 C LEU 456	45.680 15.800 5.226 1.00 20.37	PROT
	ATOM	1838 O LEU 456	46.207 16.866 5.548 1.00 29.61	PROT
	ATOM	1839 N GLU 457	44.367 15.607 5.280 1.00 13.06	PROT
30	ATOM	1840 CA GLU 457	43.483 16.675 5.713 1.00 14.14	PROT
50	ATOM	1841 CB GLU 457	42.037 16.256 5.516 1.00 29.57	PROT
	ATOM	1842 C GLU 457	43.731 17.058 7.173 1.00 14.95	PROT
	ATOM	1843 O GLU 457	43.771 18.237 7.514 1.00 15.98	PROT
	ATOM	1844 N VAL 458	43.901 16.051 8.026 1.00 26.34	PROT
35	ATOM	1845 CA VAL 458	44.143 16.260 9.455 1.00 24.39	PROT
J J	ATOM	1846 CB VAL 458	44.219 14.910 10.208 1.00 20.14	PROT
	ATOM	1847 CGI VAL 458	44.882 15.102 11.554 1.00 22.01	PROT
	ATOM		42.831 14.341 10.400 1.00 28.11	PROT
	ATOM	1849 C VAL 458	45.417 17.039 9.778 1.00 21.50	PROT
40	ATOM	1850 O VAL 458	45.364 18.062 10.439 1.00 18.85	PROT
70	ATOM	1851 N PHE 459	46.557 16.546 9.308 1.00 16.05	PROT
	ATOM	1852 CA PHE 459	47.840 17.174 9.586 1.00 20.28	PROT
	ATOM	1853 CB PHE 459	48.862 16.072 9.846 1.00 20.26	PROT
	ATOM	1854 CG PHE 459	48.389 15.055 10.833 1.00 27.22	PROT
45	ATOM	1855 CD1 PHE 459	47.917 13.822 10.408 1.00 28.01	PROT
40	ATOM	1856 CD2 PHE 459	48.390 15.339 12.204 1.00 40.66	PROT
	ATOM	1857 CEI PHE 459	47.447 12.876 11.334 1.00 21.78	PROT
	ATOM	1858 CE2 PHE 459	47.922 14.402 13.140 1.00 25.98	PROT
	ATOM	1859 CZ PHE 459	47.450 13.172 12.702 1.00 17.63	PROT
50	ATOM	1860 C PHE 459	48.381 18.152 8.540 1.00 23.03	PROT
50	AIOM	1000 C FRE 439	CO.CZ 00.1 0FC.0 2C1.01 10C.0F	1101

	ATOM	1861 O PHE 45	9	49.601 18.311 8.416 1.00 27.34 PROT
	ATOM	1862 N GLU 46	0	47.480 18.816 7.815 1.00 33.88 PROT
	ATOM	1863 CA GLU 4	60	47.846 19.774 6.767 1.00 36.60 PROT
	ATOM	1864 CB GLU 4	60	48.930 20.732 7.257 1.00 46.04 PROT
5	ATOM	1865 CG GLU 4	60	48.406 21.899 8.054 1.00 67.27 PROT
	ATOM	1866 CD GLU 4	60	47.298 22.636 7.339 1.00 71.34 PROT
	ATOM	1867 OE1 GLU 4	60	
	ATOM	1868 OE2 GLU 4	60	
	ATOM	1869 C GLU 46	0	48.353 19.037 5.535 1.00 46.31 PROT
10	ATOM	1870 O GLU 46	0	48.642 17.829 5.655 1.00 51.79 PROT
	ATOM	1871 OT GLU 4	60	48.461 19.669 4.462 1.00 60.92 PROT
	ATOM	1872 C1 GC1 1		47.011 4.539 15.912 1.00 29.38 LIGA
	ATOM	1873 C2 GC1 1		51.292 6.537 13.571 1.00 17.11 LIGA
	ATOM	1874 C3 GC1 1		47.393 4.205 14.573 1.00 33.72 LIGA
15	ATOM	1875 C4 GC1 1		52.119 6.409 12.400 1.00 19.76 LIGA
	ATOM	1876 C5 GC1 1		48.689 4.481 14.089 1.00 25.02 LIGA
	ATOM	1877 C6 GC1 1		52.344 7.525 11.539 1.00 17.51 LIGA
	ATOM	1878 C7 GC1 1		49.684 5.122 14.949 1.00 23.99 LIGA
	ATOM	1879 C8 GC1 1		51.722 8.778 11.873 1.00 20.21 LIGA
20	ATOM	1880 C9 GC1 1		49.283 5.452 16.318 1.00 18.19 LIGA
	ATOM	1881 C10 GC1	l	50.906 8.928 13.018 1.00 15.43 LIGA
	ATOM	1882 C11 GC1	1	47.973 5.163 16.779 1.00 30.64 LIGA
	ATOM	1883 C12 GC1	1	50.696 7.827 13.850 1.00 25.06 LIGA
	ATOM	1884 O5 GC1	i	45.700 4.254 16.325 1.00 28.60 LIGA
25	ATOM	1885 C14 GC1	1	53.198 7.459 10.291 1.00 20.30 LIGA
	ATOM		1	45.305 3.866 17.666 1.00 18.51 LIGA
	ATOM	1887 C16 GC1	1	52.423 6.824 9.131 1.00 17.21 LIGA
	ATOM	1888 C17 GC1	1	43.816 4.078 17.872 1.00 21.43 LIGA
	ATOM	1889 C18 GC1	1	54.514 6.689 10.543 1.00 24.97 LIGA
30	ATOM	1890 C19 GC1	1	48.994 4.093 12.664 1.00 33.46 LIGA
	ATOM	1891 C20 GC1	1	50.243 6.110 17.278 1.00 27.69 LIGA
	ATOM	1892 O1 GC1	Ì	51.902 9.861 11.086 1.00 23.34 LIGA
	ATOM	1893 C21 GC1	1	51.026 5.430 14.458 1.00 22.49 LIGA
	ATOM	1894 O3 GC1	l	43.147 3.117 18.247 1.00 18.06 LIGA
35	ATOM	1895 O4 GC1	l	43.331 5.204 17.665 1.00 28.27 LIGA
	END			

APPENDIX 8

TRBGC1.PDB

REMARK TR-beta GC-2 Full length numbering

REMARK refinement resolution: 100.00 - 2.40 A starting r= 0.2602 free_r= 0.2960

REMARK final r=0.2532 free_r=0.2894

REMARK sg= P3(1)21 a= 68.9 b= 68.9 c= 131.5 alpha= 90 beta= 90 gamma= 120

REMARK theoretical total number of refl. in resol. range: 14710 (100.0 %)

REMARK number of unobserved reflections (no entry or |F|=0): 336 (2.3 %)

REMARK number of reflections rejected:

0(0.0%)

10 REMARK total number of reflections used:

14374 (97.7 %)

REMARK number of reflections in working set:

13656 (92.8 %)

REMARK number of reflections in test set:

718 (4.9 %)

REMARK

REMARK ALA 199 to ALA 201 from His-tag

15 REMARK

5

REMARK Four cacodylate-modified cysteines (CYA)

REMARK Cys294, Cys298, Cys388, Cys434

REMARK cacodylate modeled as single arsenic atom

REMARK

20 REMARK side chain of certain residues modeled as ALA due to poor density;

REMARK however, residue name reflects true residue for clarity

REMARK

REMARK amino acid sequence confirmed,

REMARK differing from that reported by Weinberger et. al.

25 REMARK in the following codons:

REMARK 243 Pro - Arg

REMARK 337 lle - Thr

REMARK 451 Leu - Phe

REMARK as reported by Sakurai et. al.

REMARK note also correction of initiation codon,

REMARK yielding a polypeptide of 461 amino acids

JRNL AUTH A.SAKURAI, A.NAKAI, L.J.DEGROOT

JRNL TITL STRUCTURAL ANALYSIS OF HUMAN THYROID HORMONE RECEPTOR

35 JRNL TITL2 BETA GENE

JRNL REF MOL.CELL.ENDO. V.71 1990

JRNL AUTH

C.WEINBERGER,

C.C.THOMPSON,R.LEBO,D.J.GRUOL,R.M.EVANS

JRNL TITL THE C-ERB-A GENE ENCODES A THYROID HORMONE

40 RECEPTOR

JRNL REF NATURE

V.324 6098 1986

ATOM 1 CB ALA 199 36.564 26.104 43.169 1.00 73.87

ATOM 2 C ALA 199 34.723 26.996 44.613 1.00 78.22

ATOM 3 O ALA 199 34.741 28.230 44.568 1.00 81.84

45 ATOM 4 N ALA 199 34.389 26.744 42.166 1.00 77.76

ATOM 5 CA ALA 199 35.048 26.165 43.375 1.00 77.98

ATOM 6 N ALA 200 34.428 26.309 45.713 1.00 77.78

```
34.098 26.961 46.984 1.00 77.03
             7 CA ALA 200
    ATOM
                               32.761 27.693 46.865 1.00 79.04
    ATOM
             8 CB ALA 200
                              34.028 25.897 48.084 1.00 75.79
             9 C ALA 200
    ATOM
                              34.877 25.857 48.978 1.00 71.58
             10 O ALA 200
    ATOM
                              33.005 25.050 48.010 1.00 73.70
             11 N ALA 201
    ATOM
                               32.838 23.968 48.972 1.00 70.15
             12 CA ALA 201
     ATOM
                               31.468 23.328 48.809 1.00 71.16
             13 CB ALA 201
    ATOM
                              33.934 22.963 48.642 1.00 67.54
             14 C ALA 201
    ATOM
                              34.218 22.044 49.413 1.00 67.14
    ATOM
             15 O ALA 201
                              34.540 23.164 47.476 1.00 62.05
             16 N GLU 202
10
    ATOM
                               35.624 22.325 46.975 1.00 59.45
             17 CA GLU 202
     ATOM
                               35.835 22.621 45.482 1.00 55.12
             18 CB GLU 202
     ATOM
                               36.820 21.716 44.749 1.00 56.25
             19 CG GLU 202
     ATOM
                               36.382 20.260 44.723 1.00 54.99
             20 CD GLU 202
     ATOM
                                35.216 19.990 44.361 1.00 53.83
             21 OE1 GLU 202
     ATOM
15
                                37.210 19.385 45.050 1.00 59.90
             22 OE2 GLU 202
     ATOM
                               36.885 22.674 47.770 1.00 55.96
             23 C GLU 202
     ATOM
     ATOM
             24 O GLU 202
                               37.472 21.823 48.435 1.00 52.90
             25 N GLU 203
                               37.282 23.943 47.698 1.00 54.95
     ATOM
                               38.464 24.434 48.390 1.00 55.59
             26 CA GLU 203
20
     ATOM
                               38.632 25.924 48.126 1.00 53.21
             27 CB GLU 203
     ATOM
                               38.415 24.171 49.894 1.00 56.30
     ATOM
             28 C GLU 203
                               39.445 23.948 50.526 1.00 58.70
     ATOM
             29 O GLU 203
             30 N LEU 204
                               37.213 24.193 50.462 1.00 57.14
     ATOM
                               37.038 23.966 51.893 1.00 56.93
             31 CA LEU 204
     ATOM
25
                               35.658 24.465 52.338 1.00 58.31
     ATOM
             32 CB LEU 204
                               35.348 24.508 53.839 1.00 51.69
             33 CG LEU 204
     ATOM
             34 CD1 LEU 204
                                36.314 25.446 54.549 1.00 44.38
     ATOM
                                33.920 24.986 54.039 1.00 52.44
             35 CD2 LEU 204
     ATOM
                               37.198 22.489 52.246 1.00 58.20
             36 C LEU 204
30
     ATOM
                               37.831 22.155 53.252 1.00 58.99
             37 O LEU 204
     ATOM
             38 N GLN 205
                               36.620 21.607 51.431 1.00 58.26
     ATOM
                                36.736 20.167 51.657 1.00 55.38
     ATOM
             39 CA GLN 205
                                35.993 19.377 50.584 1.00 54.52
             40 CB GLN 205
     ATOM
                                34.498 19.324 50.741 1.00 53.33
             41 CG GLN 205
35
     ATOM
                                33.854 18.520 49.629 1.00 53.40
             42 CD GLN 205
     ATOM
                                33.850 18.939 48.473 1.00 51.68
             43 OE1 GLN 205
     ATOM
                                33.325 17.352 49.968 1.00 51.34
     ATOM
             44 NE2 GLN 205
                               38.200 19.775 51.608 1.00 55.05
             45 C GLN 205
     ATOM
                               38.665 18.964 52.407 1.00 53.63
40
     ATOM
             46 O GLN 205
             47 N LYS 206
                               38.918 20.348 50.648 1.00 53.55
     ATOM
                               40.337 20.078 50.493 1.00 57.40
             48 CA LYS 206
     ATOM
             49 CB LYS 206
                               40.896 20.814 49.269 1.00 58.94
     ATOM
                               40.300 20.375 47.941 1.00 67.73
             50 CG LYS 206
     ATOM
             51 CD LYS 206
                               40.921 21.141 46.781 1.00 72.50
     ATOM
45
                               40.346 20.695 45.445 1.00 75.60
             52 CE LYS 206
     ATOM
                               40.945 21.445 44.304 1.00 77.08
              53 NZ LYS 206
     ATOM
              54 C LYS 206
                               41.053 20.559 51.747 1.00 53.98-
     ATOM
                               41.905 19.866 52.300 1.00 53.49
              55 O LYS 206
     ATOM
                               40.680 21.757 52.184 1.00 53.61
              56 N SER 207
     ATOM
50
```

WO 99/26966

PCT/US98/25296

	ATOM	57 CA SER 207 41.254 22.386 53.364 1.00 51.49
	ATOM	58 CB SER 207 40.546 23.715 53.619 1.00 51.01
	ATOM	59 OG SER 207 41.108 24.383 54.731 1.00 63.00
	ATOM	60 C SER 207 41.178 21.502 54.616 1.00 49.49
5	ATOM	61 O SER 207 42.073 21.538 55.465 1.00 47.44
	ATOM	62 N ILE 208 40.117 20.707 54.725 1.00 44.39
	ATOM	63 CA ILE 208 39.938 19.829 55.874 1.00 45.99
	ATOM	64 CB ILE 208 38.421 19.627 56.174 1.00 44.50
	ATOM	65 CG2 ILE 208 38.226 18.801 57.445 1.00 49.37
10	ATOM	66 CG1 ILE 208 37.766 20.993 56.385 1.00 42.73
	ATOM	67 CD1 ILE 208 36.266 20.941 56.567 1.00 44.13
	ATOM	68 C ILE 208 40.614 18.477 55.643 1.00 47.80
	ATOM	69 O ILE 208 40.735 17.666 56.562 1.00 49.81
	ATOM	70 N GLY 209 41.059 18.238 54.412 1.00 51.31
15	ATOM	71 CA GLY 209 41.728 16.983 54.107 1.00 46.85
	ATOM	72 C GLY 209 40.813 15.896 53.573 1.00 48.31
	ATOM	73 O GLY 209 41.203 14.730 53.485 1.00 47.75
	ATOM	74 N HIS 210 39.582 16.274 53.237 1.00 46.79
	ATOM	75 CA HIS 210 38.622 15.326 52.686 1.00 47.34
20	ATOM	76 CB HIS 210 37.200 15.739 53.068 1.00 49.39
	ATOM	77 C HIS 210 38.796 15.350 51.162 1.00 45.47
	ATOM	78 O HIS 210 38.924 16.420 50.566 1.00 41.32
	ATOM	79 N LYS 211 38.829 14.176 50.545 1.00 45.76
	ATOM	80 CA LYS 211 38.991 14.095 49.090 1.00 43.42
25	ATOM	81 CB LYS 211 39.892 12.910 48.715 1.00 46.72
	ATOM	82 CG LYS 211 41.210 12.815 49.497 1.00 56.48
	ATOM	83 CD LYS 211 42.068 14.089 49.486 1.00 60.93
	ATOM	84 CE LYS 211 42.562 14.496 48.103 1.00 61.95
	ATOM	85 NZ LYS 211 41.485 15.024 47.218 1.00 69.93
30	ATOM	86 C LYS 211 37.609 13.917 48.473 1.00 35.68
	ATOM	87 O LYS 211 37.019 12.847 48.557 1.00 33.58
	ATOM	88 N PRO 212 37.077 14.972 47.828 1.00 35.64 89 CD PRO 212 37.654 16.304 47.584 1.00 38.60
	ATOM	
2.5	ATOM	
35	ATOM	·
	ATOM ATOM	
	ATOM	
40	ATOM	
40	ATOM	96 CA GLU 213 34.256 12.160 45.049 1.00 43.87 97 CB GLU 213 33.722 10.873 45.684 1.00 45.16
	ATOM	
	ATOM	
	ATOM	· · · · · -
45	ATOM	
45	ATOM	
	ATOM	
	ATOM	103 O GLU 213 32.703 13.876 44.368 1.00 43.13 104 N PRO 214 32.953 12.154 42.933 1.00 46.52
	ATOM	105 CD PRO 214 32.933 12.134 42.393 1.00 46.44
50	ATOM	105 CD PRO 214 33.439 10.884 42.391 1.00 40.44 106 CA PRO 214 31.995 12.737 41.982 1.00 47.52
50	ATOM	100 CA FRO 214 31.773 12.737 41.702 1.00 47.32

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107 CB PRO 214
                              32.040 11.750 40.813 1.00 45.40
    ATOM
                              33.445 11.181 40.913 1.00 49.89
            108 CG PRO 214
    ATOM
                             30.564 12.969 42.465 1.00 45.70
    ATOM
           109 C PRO 214
    ATOM 110 O PRO 214
                              29.972 12.112 43:121 1.00 44.49
                              30.013 14.136 42.129 1.00 45.24
    ATOM
           111 N THR 215
                             28.629 14.447 42.483 1.00 49.36
    ATOM 112 CA THR 215
    ATOM 113 CB THR 215
                              28.312 15.949 42.330 1.00 44.86
    ATOM 114 OG1 THR 215
                               28.253 16.285 40.942 1.00 52.26
                               29.387 16.793 42.992 1.00 39.43
    ATOM 115 CG2 THR 215
    ATOM 116 C THR 215
                              27.791 13.673 41.464 1.00 52.51
10
                             28.326 13.192 40.465 1.00 53.48
    ATOM 117 O THR 215
                             26.491 13.543 41.712 1.00 58.81
    ATOM 118 N ASP 216
    ATOM 119 CA ASP 216
                              25.603 12.810 40.805 1.00 61.51
                              24.150 12.941 41.270 1.00 70.57
    ATOM 120 CB ASP 216
    ATOM 121 CG ASP 216
                              23.902 12.257 42.595 1.00 78.07
15
                               24.042 11.018 42.660 1.00 82.31
    ATOM 122 OD1 ASP 216
                               23.572 12.962 43.571 1.00 86.55
    ATOM 123 OD2 ASP 216
                             25.706 13.277 39.356 1.00 58.42
    ATOM 124 C ASP 216
    ATOM 125 O ASP 216
                             25.695 12.464 38.429 1.00 56.85
    ATOM 126 N GLU 217
                              25.798 14.587 39.167 1.00 54.92
20
                              25.905 15.156 37.833 1.00 53.37
    ATOM 127 CA GLU 217
                              25.861 16.682 37.906 1.00 51.02
           128 CB GLU 217
    ATOM
    ATOM 129 C GLU 217
                              27.211 14.692 37.195 1.00 53.55
    ATOM 130 O GLU 217
                              27.239 14.301 36.027 1.00 54.33
                              28.290 14.726 37.975 1.00 49.20
    ATOM 131 N GLU 218
25
                              29.593 14.310 37.486 1.00 45.94
    ATOM 132 CA GLU 218
                               30.674 14.601 38.530 1.00 43.43
    ATOM 133 CB GLU 218
                               30.787 16.069 38.878 1.00 40.86
    ATOM 134 CG GLU 218
    ATOM 135 CD GLU 218
                               31.930 16.347 39.826 1.00 39.88
                               32.000 15.667 40.875 1.00 37.61
    ATOM 136 OE1 GLU 218
30
                               32.748 17.250 39.529 1.00 34.01
    ATOM 137 OE2 GLU 218
                              29.624 12.838 37.101 1.00 44.71
    ATOM 138 C GLU 218
                              30.275 12.471 36.130 1.00 45.31
    ATOM 139 O GLU 218
    ATOM 140 N TRP 219
                              28.935 11.991 37.863 1.00 44.02
                              28.892 10.572 37.539 1.00 46.97
    ATOM 141. CA TRP 219
35
                              28.183 9.762 38.630 1.00 48.42
    ATOM 142 CB TRP 219
                               29.034 9.473 39.823 1.00 54.61
     ATOM 143 CG TRP 219
                               30.167 8.572 39.879 1.00 55.24
     ATOM 144 CD2 TRP 219
    ATOM 145 CE2 TRP 219
                               30.659 8.610 41.201 1.00 53.67
                               30.795 7.745 38.938 1.00 54.55
    ATOM 146 CE3 TRP 219
                               28.902 10.000 41.074 1.00 55.75
     ATOM 147 CD1 TRP 219
                               29.868 9.491 41.912 1.00 54.43
     ATOM 148 NE1 TRP 219
                               31.771 7.846 41.622 1.00 52.54
           149 CZ2 TRP 219
     ATOM
                               31.912 6.975 39.353 1.00 55.17
            150 CZ3 TRP 219
     ATOM
                               32.380 7.038 40.690 1.00 55.59
     ATOM
           151 CH2 TRP 219
45
                              28.167 10.356 36.216 1.00 47.32
     ATOM 152 C TRP 219
                              28,433 9,384 35,503 1,00 43,56
     ATOM 153 O TRP 219
                              27.247 11.259 35.898 1.00 49.91
     ATOM 154 N GLU 220
           155 CA GLU 220
                               26.497 11.155 34.655 1.00 53.57
     ATOM
                               25.274 12.075 34.694 1.00 58.18
     ATOM 156 CB GLU 220
50
```

```
157 CG GLU 220
                               24.323 11.876 33.526 1.00 73.13
    ATOM
                               23.082 12.742 33.630 1.00 80.06
            158 CD GLU 220
    ATOM
                                22.348 12.619 34.636 1.00 82.12
            159 OE1 GLU 220
    ATOM
            160 OE2 GLU 220
                                22.839 13.545 32.701 1.00 82.78
    ATOM
                              27.419 11.534 33.497 1.00 50.51
    ATOM
            161 C GLU 220
                              27.399 10.899 32.443 1.00 49.94
            162 O GLU 220
    ATOM
                              28.232 12.567 33.711 1.00 43.71
    ATOM 163 N LEU 221
                               29.187 13.019 32.702 1.00 42.81
    ATOM
            164 CA LEU 221
                               29.868 14.317 33.155 1.00 39.21
    ATOM 165 CB LEU 221
           166 CG LEU 221
                               30.945 14.949 32.261 1.00 36.34
    ATOM
10
                                30.339 15.351 30.922 1.00 36.93
           167 CD1 LEU 221
    ATOM
            168 CD2 LEU 221
                                31.535 16.164 32.949 1.00 24.18
    ATOM
           169 C LEU 221
                              30.234 11.928 32.505 1.00 43.46
    ATOM
           170 O LEU 221
                              30.618 11.621 31.375 1.00 45.25
    ATOM
            171 N ILE 222
                              30.683 11.342 33.614 1.00 39.09
15
    ATOM
                              31.677 10.273 33.586 1.00 35.47
            172 CA ILE 222
     ATOM
           173 CB ILE 222
                              32.031 9.811 35.037 1.00 33.74
     ATOM
                               32.822 8.505 35.018 1.00 28.86
            174 CG2 ILE 222
    ATOM
    ATOM 175 CG1 ILE 222
                               32.813 10.918 35.745 1.00 33.33
    ATOM 176 CD1 ILE 222
                               33.111 10.646 37.199 1.00 34.85
20
                              31.139 9.098 32.781 1.00 34.26
     ATOM 177 C ILE 222
                              31.877 8.427 32.070 1.00 31.90
    ATOM 178 O ILE 222
                              29.840 8.860 32.908 1.00 39.49
     ATOM 179 N LYS 223
                               29.168 7.775 32.210 1.00 44.43
     ATOM 180 CA LYS 223
           181 CB LYS 223
                               27.696 7.733 32.635 1.00 50.81
25
     ATOM
                               26.845 6.693 31.929 1.00 62.51
            182 CG LYS 223
     ATOM
     ATOM 183 CD LYS 223
                               25.379 6.856 32.313 1.00 72.22
                               24.487 5.855 31.591 1.00 74.55
     MOTA
            184 CE LYS 223
            185 NZ LYS 223
                               23.045 6.057 31.925 1.00 75.78
     ATOM
                              29.266 7.983 30.691 1.00 42.81
            186 C LYS 223
30
     ATOM
                              29.640 7.078 29.946 1.00 40.36
            187 O LYS 223
     ATOM
                               28.924 9.194 30.257 1.00 39.89
     ATOM
            188 N THR 224
            189 CA THR 224
                               28.948 9.566 28.850 1.00 39.93
     ATOM
            190 CB THR 224
     ATOM
                               28.466 11.021 28.680 1.00 40.57
                                27.135 11.134 29.197 1.00 39.27
            191 OG1 THR 224
35
     ATOM
                                28.480 11.437 27.214 1.00 38.11
           192 CG2 THR 224
     ATOM
                               30.333 9.433 28.234 1.00 39.96
           193 C THR 224
     ATOM
                               30.515 8.714 27.248 1.00 36.67
           194 O THR 224
     ATOM
                               31.303 10.123 28.833 1.00 38.02
            195 N VAL 225
     ATOM
                                32.680 10.117 28.355 1.00 38.12
            196 CA VAL 225
     ATOM
                                33.565 11.014 29.243 1.00 38.19
     ATOM 197 CB VAL 225
            198 CG1 VAL 225
                                34.960 11.162 28.632 1.00 36.77
     ATOM
                                32.910 12.361 29.406 1.00 41.76
     ATOM 199 CG2 VAL 225
                               33.291 8.724 28.302 1.00 37.52
     ATOM 200 C VAL 225
                               34.022 8.395 27.364 1.00 36.77
     ATOM 201 O VAL 225
45
                               33.002 7.904 29.310 1.00 34.02
     ATOM 202 N THR 226
                               33.542 6.552 29.350 1.00 34.67
     ATOM 203 CA THR 226
                                33.237 5.857 30.707 1.00 30.56
     ATOM 204 CB THR 226
     ATOM 205 OG1 THR 226
                                33.858 6.598 31.768 1.00 32.20
     ATOM 206 CG2 THR 226
                                33.775 4.437 30.722 1.00 20.99
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207 C THR 226
                              32.960 5.722 28.211 1.00 36.41
    ATOM
                              33.698 5.075 27.472 1.00 39.64
    ATOM
           208 O THR 226
           209 N GLU 227
                              31.636 5.758 28.073 1.00 39.20
    ATOM
                               30.935 5.020 27.027 1.00 36.93
           210 CA GLU 227
    ATOM
                              29.434 5.296 27.111 1.00 38.06
    ATOM 211 CB GLU 227
    ATOM 212 C GLU 227
                              31.466 5.409 25.651 1.00 37.69
    ATOM 213 O GLU 227
                              31.713 4.544 24.805 1.00 40.94
                              31.641 6.709 25.439 1.00 32.86
    ATOM 214 N ALA 228
                               32.156 7.236 24.177 1.00 32.48
    ATOM 215 CA ALA 228
    ATOM 216 CB ALA 228
                               32.285 8.746 24.256 1.00 28.25
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    ATOM 217 C ALA 228
                              33.508 6.612 23.861 1.00 36.12
                              33.736 6.135 22.747 1.00 37.86
    ATOM 218 O ALA 228
    ATOM 219 N HIS 229
                             34.404 6.611 24.843 1.00 33.58
    ATOM 220 CA HIS 229
                              35.724 6.029 24.669 1.00 32.97
    ATOM 221 CB HIS 229
                              36.579 6.263 25.921 1.00 33.69
15
                              37.857 5.489 25.934 1.00 28.39
           222 CG HIS 229
    ATOM
                              38.338 4.576 26.811 1.00 28.83
    ATOM 223 CD2 HIS 229
                              38.804 5.593 24.937 1.00 30.47
    ATOM
           224 ND1 HIS 229
           225 CE1 HIS 229
                              39.812 4.779 25.193 1.00 26.95
    ATOM
                              39.556 4.147 26.332 1.00 31.27
    ATOM 226 NE2 HIS 229
20
                             35.653 4.536 24.371 1.00 38.40
    ATOM 227 C HIS 229
    ATOM 228 O HIS 229
                             36.227 4.071 23.383 1.00 41.49
                              34.951 3.786 25.216 1.00 38.55
    ATOM 229 N VAL 230
    ATOM 230 CA VAL 230
                               34.823 2.339 25.049 1.00 40.40
                               33,964 1.726 26.196 1.00 44.68
    ATOM 231 CB VAL 230
25
                               33.865 0.208 26.041 1.00 39.39
    ATOM 232 CG1 VAL 230
                               34.576 2.075 27.540 1.00 42.18
    ATOM 233 CG2 VAL 230
    ATOM 234 C VAL 230
                              34.219 1.934 23.700 1.00 44.28 .
                              34.640 0.948 23.092 1.00 45.94
    ATOM 235 O VAL 230
                              33.236 2.698 23.230 1.00 45.59
    ATOM 236 N ALA 231
30
                               32.580 2.403 21.961 1.00 47.84
     ATOM 237 CA ALA 231
                              31.297 3.227 21.832 1.00 45.08
    ATOM 238 CB ALA 231
                              33.487 2.666 20.761 1.00 48.04
    ATOM 239 C ALA 231
                              33.364 2.012 19.727 1.00 49.95
    ATOM 240 O ALA 231
     ATOM 241 N THR 232
                              34,403 3.619 20.907 1.00 47.26
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                               35.312 3.973 19.824 1.00 43.64
     ATOM 242 CA THR 232
                               35.379 5.502 19.629 1.00 41.93
    ATOM 243 CB THR 232
     ATOM 244 OG1 THR 232
                               35.945 6.117 20.797 1.00 39.10
                               33.985 6.065 19.382 1.00 29.80
     ATOM 245 CG2 THR 232
                              36.720 3.458 20.046 1.00 43.97
     ATOM
           246 C THR 232
40
                              37.629 3.791 19.292 1.00 40.55
     ATOM
           247 O THR 232
                              36.905 2.648 21.081 1.00 48.62
     ATOM
           248 N ASN 233
                               38.218 2.101 21.368 1.00 58.62
     ATOM
           249 CA ASN 233
                               38.473 2.092 22.876 1.00 62.44
     ATOM
           250 CB ASN 233
           251 CG ASN 233
                               39.909 1.765 23.223 1.00 68.35
45
     ATOM
                               40.843 2.401 22.724 1.00 65.50
           252 OD1 ASN 233
     ATOM
                               40.098 0.776 24.090 1.00 74.29
     ATOM 253 ND2 ASN 233
                              38,282 0.690 20.802 1.00 65.06
     ATOM 254 C ASN 233
                              37.748 -0.257 21.382 1.00 69.47
     ATOM 255 O ASN 233
     ATOM 256 N ALA 234
                              38.934 0.577 19.645 1.00 68.80
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ATOM 257 CA ALA 234
                               39.098 -0.672 18.909 1.00 70.98
                               40.215 -0.508 17.886 1.00 71.43
    ATOM 258 CB ALA 234
    ATOM 259 C ALA 234
                               39.353 -1.919 19.753 1.00 73.83
    ATOM 260 O ALA 234
                               40.193 -1.911 20.652 1.00 74.33
    ATOM 261 N GLN 235
                               38.615 -2.983 19.434 1.00 75.07
    ATOM 262 CA GLN 235
                               38.720 -4.281 20.103 1.00 76.32
    ATOM 263 CB GLN 235
                               40.130 -4.856 19.912 1.00 76.98
                               40.429 -5.417 18.516 1.00 77.07
    ATOM 264 CG GLN 235
                                40.142 -4.444 17.377 1.00 80.85
    ATOM 265 CD GLN 235
    ATOM 266 OE1 GLN 235
                                38.985 -4.144 17.072 1.00 82.01
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    ATOM 267 NE2 GLN 235
                                41.201 -3.949 16.742 1.00 78.80
    ATOM 268 C GLN 235
                               38.351 -4.293 21.586 1.00 77.15
    ATOM 269 O GLN 235
                               38.217 -5.361 22.190 1.00 76.06
    ATOM 270 N GLY 236
                               38.188 -3.103 22.161 1.00 77.46
    ATOM 271 CA GLY 236
                               37.818 -2.974 23.562 1.00 78.37
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    ATOM 272 C GLY 236
                               38.620 -3.783 24.566 1.00 79.43
    ATOM 273 O GLY 236
                               39.826 -3.575 24.736 1.00 79.47
                              37.937 -4.711 25.234 1.00 77.98
    ATOM 274 N SER 237
    ATOM 275 CA SER 237
                               38.544 -5.561 26.253 1.00 76.49
    ATOM 276 CB SER 237
                               37.475 -6.462 26.874 1.00 76.46
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    ATOM 277 C SER 237
                              39.712 -6.412 25.765 1.00 75.35
                              40.858 -6.181 26.152 1.00 75.47
    ATOM 278 O SER 237
    ATOM 279 N HIS 238
                              39.421 -7.397 24.922 1.00 75.56
     ATOM 280 CA HIS 238
                              40.451 -8.294 24.409 1.00 75.46
                              39.837 -9.654 24.076 1.00 75.85
    ATOM 281 CB HIS 238
25
                              41.185 -7.751 23.191 1.00 74.10
    ATOM 282 C HIS 238
    ATOM 283 O HIS 238
                              40.610 -7.638 22.109 1.00 75.34
                              42.459 -7.417 23.381 1.00 73.39
    ATOM 284 N TRP 239
     ATOM 285 CA TRP 239
                               43.300 -6.907 22.302 1.00 74.02
    ATOM 286 CB TRP 239
                               43.556 -5.402 22.460 1.00 81.77
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    ATOM 287 CG TRP 239
                               44.190 -5.023 23.761 1.00 89.67
                               45.597 -4.797 24.008 1.00 93.19
    ATOM 288 CD2 TRP 239
    ATOM 289 CE2 TRP 239
                               45.744 -4.527 25.384 1.00 95.46
    ATOM 290 CE3 TRP 239
                               46.732 -4.793 23.186 1.00 95.35
     ATOM 291 CD1 TRP 239
                                43.566 -4.888 24.972 1.00 94.16
35
                                44.483 -4.591 25.954 1.00 97.48
    ATOM 292 NE1 TRP 239
                                46,993 -4.262 25.981 1.00 96.23
    ATOM 293 CZ2 TRP 239
     ATOM 294 CZ3 TRP 239
                               47.992 -4.528 23.778 1.00 96.75
     ATOM 295 CH2 TRP 239
                                48.101 -4.262 25.164 1.00 97.32
     ATOM 296 C TRP 239
                              44.633 -7.649 22.283 1.00 70.77
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                              45.339 -7.644 21.274 1.00 71.70
     ATOM 297 O TRP 239
     ATOM 298 N LYS 240
                               44.978 -8.276 23.405 1.00 67.10
     ATOM 299 CA LYS 240
                               46.219 -9.040 23.519 1.00 65.63
     ATOM 300 CB LYS 240
                               46.387 -9.569 24.946 1.00 66.65
     ATOM 301 CG LYS 240
                               46.379 -8.504 26.030 1.00 69.83
45
     ATOM 302 CD LYS 240
                               47.664 -7.691 26.069 1.00 71.49
                               48.839 -8.515 26.573 1.00 71.31
     ATOM 303 CE LYS 240
     ATOM 304 NZ LYS 240
                               50.071 -7.684 26.691 1.00 72.23
                              46.143 -10.222 22.555 1.00 66.19
     ATOM 305 C LYS 240
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     ATOM 306 O LYS 240
                              47.075 -10.493 21.797 1.00 65.20
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45.010 -10.923 22.598 1.00 66.69
             307 N ASN 241
      ATOM
                                 44.773 -12.089 21.750 1.00 67.53
             308 CA ASN 241
      ATOM
                                 43.503 -12.813 22.213 1.00 67.98
             309 CB ASN 241
      ATOM
                                 43.504 -13.096 23.704 1.00 70.19
      ATOM 310 CG ASN 241
                                 44.410 -13.744 24.227 1.00 71.37
      ATOM 311 OD1 ASN 241
      ATOM 312 ND2 ASN 241
                                 42.483 -12.605 24.400 1.00 71.48
                                44.621 -11.681 20.286 1.00 66.62
      ATOM 313 C ASN 241
                                44.882 -12.475 19.382 1.00 64.76
      ATOM 314 O ASN 241
      ATOM 315 N LYS 242
                                44.196 -10.436 20.070 1.00 66.86
                                43.989 -9.882 18.732 1.00 67.46
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      ATOM 316 CA LYS 242
      ATOM 317 CB LYS 242
                                42.982 -8.731 18.799 1.00 67.93
                                 41.601 -9.138 19.279 1.00 71.52
      ATOM 318 CG LYS 242
             319 CD LYS 242
                                 40.876 -9.986 18.246 1.00 74.32
      ATOM
      ATOM 320 CE LYS 242
                                40.449 -9.160 17.043 1.00 74.41
                                39.455 -8.120 17.436 1.00 74.44
      ATOM 321 NZ LYS 242
 15
                                45.281 -9.367 18.097 1.00 66.28
      ATOM 322 C LYS 242
                                45.414 -9.334 16.874 1.00 67.61
      ATOM 323 O LYS 242
      ATOM 324 N ARG 243
                                46.225 -8.961 18.938 1.00 64.19
      ATOM 325 CA ARG 243
                                 47.497 -8.422 18.478 1.00 62.43
                                 48.376 -8.070 19.685 1.00 60.12
             326 CB ARG 243
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      ATOM
                                48.261 -9.348 17.538 1.00 62.97
      ATOM 327 C ARG 243
                                48.585 -10.484 17.891 1.00 63.96
      ATOM 328 O ARG 243
      ATOM
            329 N LYS 244
                                48.531 -8.853 16.334 1.00 62.41
                                 49.303 -9.593 15.339 1.00 61.57
      ATOM 330 CA LYS 244
                                 48.601 -9.607 13.972 1.00 63.68
      ATOM 331 CB LYS 244
 25
                                 47.210 -10.231 13.970 1.00 71.29
      ATOM 332 CG LYS 244
      ATOM 333 CD LYS 244
                                 46.666 -10.441 12.549 1.00 73.83
      ATOM 334 CE LYS 244
                                 46.505 -9.139 11.767 1.00 74.71
                                45.542 -8.199 12.407 1.00 73.32
      ATOM 335 NZ LYS 244
                                50.613 -8.824 15.223 1.00 59.30
      ATOM 336 C LYS 244
 30
                                50.637 -7.716 14.686 1.00 56.34
      ATOM 337 O LYS 244
      ATOM 338 N PHE 245
                                51.690 -9.405 15.744 1.00 57.06
                                 52.996 -8.757 15.704 1.00 59.01
      ATOM 339 CA PHE 245
                                 54.034 -9.588 16.467 1.00 59.62
      ATOM 340 CB PHE 245
                                 53,704 -9.783 17.934 1.00 66.60
      ATOM 341 CG PHE 245
 35
      ATOM 342 CD1 PHE 245
                                 52.656 -10.626 18.329 1.00 67.17
      ATOM 343 CD2 PHE 245
                                 54.427 -9.096 18.918 1.00 69.25
                                 52.320 -10.789 19.699 1.00 69.92
      ATOM 344 CE1 PHE 245
                                 54.111 -9.240 20.294 1.00 70.50
      ATOM 345 CE2 PHE 245
                                 53.051 -10.091 20.686 1.00 70.89
      ATOM 346 CZ PHE 245
 40
                                53.463 -8.537 14.272 1.00 60.68
              347 C PHE 245
      ATOM
                                53.433 -9.455 13.447 1.00 62.37
              348 O PHE 245
      ATOM
                                53.880 -7.311 13.976 1.00 60.10
      ATOM 349 N LEU 246
                                 54.359 -6.968 12.642 1.00 59.44
      ATOM 350 CA LEU 246
                                 54.654 -5.464 12.560 1.00 57.43
      ATOM 351 CB LEU 246
 45
                                 54.937 -4.851 11.183 1.00 54.41
      ATOM 352 CG LEU 246
                                 53.681 -4.931 10.320 1.00 52.43
      ATOM 353 CD1 LEU 246
                                 55.358 -3.398 11.343 1.00 51.69
      ATOM 354 CD2 LEU 246
                                55.638 -7.772 12.425 1.00 62.05
      ATOM 355 C LEU 246
                                56.447 -7.923 13.346 1.00 59.85
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      ATOM 356 O LEU 246
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357 N PRO 247
                               55.836 -8.312 11.203 1.00 63.33
    ATOM
            358 CD PRO 247
                               54.990 -8.230 10.001 1.00 64.44
    ATOM
                               57.036 -9.102 10.910 1.00 63.56
            359 CA PRO 247
    ATOM
                               56.917 -9.327 9.404 1.00 64.42
    ATOM
           360 CB PRO 247
                               55.413 -9.481 9.251 1.00 64.90
           361 CG PRO 247
    ATOM
                              58.342 -8.431 11.325 1.00 61.94
            362 C PRO 247
    ATOM
           363 O PRO 247
    ATOM
                               58.581 -7.256 11.053 1.00 61.60
                               59.180 -9.219 11.990 1.00 61.33
    ATOM 364 N ALA 248
                               60.468 -8.785 12.511 1.00 63.50
           365 CA ALA 248
    ATOM
           366 CB ALA 248
                               61.151 -9.991 13.174 1.00 66.94
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    ATOM
                               61.412 -8.140 11.489 1.00 64.19
           370 C ALA 248
    ATOM
    ATOM
            371 O ALA 248
                               62.449 -7.593 11.867 1.00 65.56
                              61.055 -8.188 10.207 1.00 64.36
            372 N ASP 249
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                               61.900 -7.610 9.163 1.00 63.33
           373 CA ASP 249
    ATOM
           374 CB ASP 249
                               62.104 -8.618 8.026 1.00 62.97
    ATOM
15
                               60.798 -9.051 7.395 1.00 64.63
            375 CG ASP 249
    ATOM
                                60.037 -9.803 8.043 1.00 64.84
    ATOM
           376 OD1 ASP 249
           377 OD2 ASP 249
                                60.526 -8.626 6.253 1.00 66.52
    ATOM
                              61.388 -6.293 8.572 1.00 64.31
           378 C ASP 249
    ATOM
    ATOM 379 O ASP 249
                              62.112 -5.624 7.830 1.00 64.73
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                              60.148 -5.927 8.885 1.00 63.09
           380 N ILE 250
    ATOM
    ATOM 381 CA ILE 250
                              59.577 -4.676 8.385 1.00 64.39
           382 CB ILE 250
                              58.035 -4.741 8.349 1.00 65.79
    ATOM
                               57.463 -3.408 7.861 1.00 64.78
           383 CG2 ILE 250
    ATOM
                               57.594 -5.893 7.439 1.00 65.28
           384 CG1 ILE 250
25
    ATOM
                               56.094 -6.103 7.362 1.00 65.08
    ATOM
           385 CD1 ILE 250
            386 C ILE 250
                              60.015 -3.534 9.299 1.00 65.21
     ATOM
                              60.002 -3.676 10.524 1.00 64.05
    ATOM
           387 O ILE 250
                               60.401 -2.405 8.700 1.00 65.48
            388 N GLY 251
     ATOM
                               60.864 -1.263 9.472 1.00 67.32
           389 CA GLY 251
30
     ATOM
                               62.069 -1.711 10.271 1.00 68.52
     ATOM
           390 C GLY 251
    ATOM
                               62.099 -1.610 11.497 1.00 65.49
           391 O GLY 251
     ATOM
            392 N GLN 252
                               63.080 -2.194 9.555 1.00 72.26
                               64.277 -2.726 10.176 1.00 74.10
           393 CA GLN 252
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                               64.598 -4.068 9.515 1.00 75.82
    ATOM 394 CB GLN 252
35
                                65.518 -4.974 10.302 1.00 77.81
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                                65.686 -6.319 9.630 1.00 79.38
     ATOM 396 CD GLN 252
                                66.087 -6.397 8.468 1.00 80.55
     ATOM
           397 OE1 GLN 252
           398 NE2 GLN 252
                                65.384 -7.391 10.357 1.00 78.12
     ATOM
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     ATOM
           399 C GLN 252
                               65.496 -1.817 10.138 1.00 77.17
            400 O GLN 252
                               65.553 -0.826 9.399 1.00 76.50
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                               66,470 -2.187 10.966 1.00 80.78
            401 N ALA 253
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                                67.729 -1.475 11.104 1.00 83.70
     ATOM
            402 CA ALA 253
                                68.402 -1.903 12.401 1.00 83.23
     ATOM
            403 CB ALA 253
            404 C ALA 253
                               68.639 -1.774 9.913 1.00 85.59
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     ATOM
                               68.294 -2.673 9.117 1.00 85.69
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            405 O ALA 253
                                 69.694 -1.115 9.802 1.00 88.37
     ATOM
            406 OXT ALA 253
            429 CB LYS 263
                               65.708 7.766 4.514 1.00 63.50
     ATOM
            430 C LYS 263
                               64.141 6.903 6.272 1.00 63.41
     ATOM
            431 O LYS 263
                               64.442 5.776 6.673 1.00 61.93
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     ATOM
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66.368 7.841 6.894 1.00 61.71
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    ATOM
                              65.218 7.942 5.950 1.00 64.36
           433 CA LYS 263
    ATOM
           434 N VAL 264
                              62.886 7.305 6.090 1.00 61.15
    ATOM
           435 CA VAL 264
                              61.724 6.462 6.351 1.00 59.46
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                               60.429 7.221 5.962 1.00 59.03
           436 CB VAL 264
    ATOM
           437 CG1 VAL 264
                               59.200 6.421 6.363 1.00 53.79
    ATOM
    ATOM
           438 CG2 VAL 264
                               60.422 8.593 6.623 1.00 55.32
                              61.790 5.129 5.595 1.00 60.96
    ATOM
           439 C VAL 264
           440 O VAL 264
                              62.071 5.098 4.395 1.00 62.13
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           441 N ASP 265
                              61.522 4.034 6.304 1.00 62.59
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    ATOM
                              61.562 2.693 5.727 1.00 64.95
           442 CA ASP 265
    ATOM
           443 CB ASP 265
                              61.322 1.644 6.810 1.00 64.32
    ATOM
                              61.415 0.232 6.277 1.00 67.70
           444 CG ASP 265
    ATOM
    ATOM 445 OD1 ASP 265
                               62.514 -0.158 5.831 1.00 72.59
    ATOM 446 OD2 ASP 265
                               60.393 -0.486 6.289 1.00 68.84
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    ATOM 447 C ASP 265
                             60.560 2.470 4.591 1.00 65.64
    ATOM 448 O ASP 265
                              60.789 1.637 3.717 1.00 68.81
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                              59.456 3.211 4.624 1.00 65.12
    ATOM 450 CA LEU 266
                              58.394 3.138 3.615 1.00 63.40
                              58.963 3.333 2.202 1.00 67.34
    ATOM 451 CB LEU 266
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    ATOM 452 CG LEU 266
                               59.665 4.662 1.894 1.00 69.35
                               60.193 4.627 0.469 1.00 68.24
    ATOM 453 CD1 LEU 266
    ATOM 454 CD2 LEU 266
                               58.705 5.831 2.075 1.00 70.47
                              57.562 1.854 3.658 1.00 59.67
    ATOM 455 C LEU 266
                              56,342 1.903 3.486 1.00 53.35
    ATOM 456 O LEU 266
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    ATOM
           457 N GLU 267
                              58.205 0.713 3.872 1.00 58.01
                               57.454 -0.535 3.945 1.00 58.34
            458 CA GLU 267
    ATOM
           459 CB GLU 267
                               58.387 -1.750 3.921 1.00 59.21
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                               57.640 -3.072 4.053 1.00 62.89
    ATOM 460 CG GLU 267
                               58.548 -4.285 3.979 1.00 67.66
    ATOM 461 CD GLU 267
30
                               59.513 -4.371 4.771 1.00 69.95
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           462 OE1 GLU 267
                               58.285 -5.162 3.129 1.00 69.40
    ATOM
           463 OE2 GLU 267
            464 C GLU 267
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                              55.488 -0.877 5.276 1.00 58.34
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           466 N ALA 268
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    ATOM 467 CA ALA 268
                               56.701 0.013 7.629 1.00 49.00
                               57.766 0.244 8.695 1.00 45.72
    ATOM 468 CB ALA 268
                              55.701 1.166 7.611 1.00 45.76
    ATOM 469 C ALA 268
                              54.598 1.057 8.144 1.00 41.50
           470 O ALA 268
    ATOM
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           471 N PHE 269
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           472 CA PHE 269
                               55,277 3,457 6.855 1.00 43.96
     ATOM
                               56.016 4.511 6.022 1.00 40.10
     ATOM 473 CB PHE 269
                               55.264 5.818 5.859 1.00 40.44
     ATOM 474 CG PHE 269
                               55.102 6.690 6.949 1.00 38.98
     ATOM
           475 CD1 PHE 269
                               54.706 6.170 4.626 1.00 37.15
45
            476 CD2 PHE 269
     ATOM
            477 CEI PHE 269
                               54.401 7.920 6.807 1.00 32.12
     ATOM
                               53.999 7.389 4.457 1.00 38.41
            478 CE2 PHE 269
     ATOM
                              53.843 8.269 5.554 1.00 40.55
     ATOM
            479 CZ PHE 269
                              53.976 3.081 6.151 1.00 49.76
            480 C PHE 269
     ATOM
                              52.903 3.622 6.443 1.00 52.15
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     ATOM 481 O PHE 269
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482 N SER 270
                              54.089 2.140 5.217 1.00 53.15
    ATOM
                              52.957 1.669 4.432 1.00 52.29
    ATOM
            483 CA SER 270
            484 CB SER 270
                              53.456 0.703 3.349 1.00 51.85
    ATOM
           485 OG SER 270
                             52,400 0.297 2.499 1.00 53.42
    ATOM
            486 C SER 270
                             51.901 0.992 5.303 1.00 49.38
    ATOM
            487 O SER 270
                              50.713 1.284 5.185 1.00 48.74
    ATOM
            488 N HIS 271
                             52.335 0.085 6.173 1.00 50.15
    ATOM
                            51.410 -0.614 7.061 1.00 51.67
            489 CA HIS 271
    ATOM
           490 CB HIS 271
                              52.150 -1.682 7.878 1.00 58.52
    ATOM
    ATOM 491 CG HIS 271
                              52.697 -2.808 7.059 1.00 68.97
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                             52.425 -4.131 7.063 1.00 70.88
           492 CD2 HIS 271
    ATOM
                               53.660 -2.621 6.080 1.00 71.98
           493 ND1 HIS 271
    ATOM
                              53.951 -3.782 5.528 1.00 73.91
           494 CE1 HIS 271
    ATOM
           495 NE2 HIS 271
                             53.214 -4.720 6.104 1.00 73.59
    ATOM
           496 C HIS 271
                             50.711 0.365 8.008 1.00 48.33
    ATOM
15
                             49.507 0.260 8.240 1.00 48.39
           497 O HIS 271
    ATOM
           498 N PHE 272
                              51.472 1.321 8.537 1.00 41.34
    ATOM
           499 CA PHE 272
                               50.946 2.316 9.462 1.00 39.44
    ATOM
    ATOM 500 CB PHE 272
                               52.076 3.215 9.976 1.00 36.67
                               53.167 2.475 10.749 1.00 33.39
    ATOM 501 CG PHE 272
20
    ATOM 502 CD1 PHE 272
                               54.421 3.065 10.915 1.00 33.14
           503 CD2 PHE 272
                               52.934 1.216 11.311 1.00 38.28
    ATOM
    ATOM 504 CE1 PHE 272
                               55.454 2.418 11.633 1.00 38.26
    ATOM 505 CE2 PHE 272
                               53.961 0.538 12.047 1.00 43.28
                               55.225 1.146 12.207 1.00 39.74
    ATOM 506 CZ PHE 272
25
    ATOM 507 C PHE 272
                              49.857 3.183 8.822 1.00 40.75
                              48.784 3.361 9.394 1.00 35.51
    ATOM 508 O PHE 272
           509 N THR 273
                              50.136 3.714 7.635 1.00 41.64
    ATOM
                               49.170 4.561 6.938 1.00 45.97
           510 CA THR 273
     ATOM
    ATOM 511 CB THR 273
                               49.813 5.249 5.711 1.00 51.52
30
                               50.339 4.257 4.815 1.00 45.74
     ATOM 512 OG1 THR 273
     ATOM 513 CG2 THR 273
                               50.936 6.179 6.158 1.00 49.73
                              47.941 3.772 6.481 1.00 46.23
     ATOM
           514 C THR 273
                              46.879 4.344 6.233 1.00 41.21
     ATOM 515 O THR 273
                              48.090 2.455 6.380 1.00 46.21
           516 N LYS 274
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    ATOM
                              46.984 1.608 5.955 1.00 54.53
     ATOM
           517 CA LYS 274
     ATOM 518 CB LYS 274
                               47.482 0.180 5.708 1.00 54.36
                              45.878 1.595 7.006 1.00 56.88
     ATOM 519 C LYS 274
                              44.695 1.486 6.675 1.00 57.98
     ATOM 520 O LYS 274
                             46.267 1.718 8.268 1.00 56.48
           521 N ILE 275
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     ATOM
     ATOM 522 CA ILE 275
                              45.312 1.695 9.368 1.00 52.64
     ATOM 523 CB ILE 275
                              45.710 0.611 10.391 1.00 49.15
                               45.719 -0.758 9.701 1.00 47.42
     ATOM 524 CG2 ILE 275
     ATOM 525 CG1 ILE 275
                               47.101 0.921 10.971 1.00 45.31
     ATOM 526 CD1 ILE 275
                               47.565 -0.050 12.053 1.00 37.22
45
                             45.175 3.032 10.086 1.00 51.78
     ATOM 527 C ILE 275
                             44.578 3.108 11.159 1.00 49.80
     ATOM 528 O ILE 275
                             45.710 4.088 9.481 1.00 51.76
     ATOM 529 N ILE 276
     ATOM 530 CA ILE 276
                            45.657 5.416 10.084 1.00 52.58
     ATOM 531 CB ILE 276
                            46.733 6.364 9.464 1.00 55.04
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46.395 6.696 8.020 1.00 53.28
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    ATOM
                               46.823 7.663 10.270 1.00 57.31
            533 CG1 ILE 276
    ATOM
            534 CD1 ILE 276
                               47.364 7.485 11.664 1.00 60.32
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                             44.279 6.073 9.974 1.00 50.70
           535 C ILE 276
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                              43.858 6.775 10.895 1.00 55.55
            536 O ILE 276
    ATOM
                              43.576 5.849 8.866 1.00 47.33
           537 N THR 277
    ATOM
                               42.255 6.450 8.681 1.00 42.59
    ATOM
           538 CA THR 277
                               41.695 6.190 7.254 1.00 44.97
            539 CB THR 277
    ATOM
                                42.611 6.702 6.280 1.00 46.38
           540 OG1 THR 277
    ATOM
           541 CG2 THR 277
                                40.349 6.892 7.065 1.00 37.17
    ATOM
10
                              41.252 5.954 9.718 1.00 39.84
            542 C THR 277
    ATOM
                              40.570 6.759 10.351 1.00 40.55
    ATOM
            543 O THR 277
                              41.126 4.620 9.899 1.00 38.20
    ATOM
            544 N PRO 278
           545 CD PRO 278
                               41.746 3.457 9.242 1.00 36.34
    ATOM
                               40.165 4.167 10.907 1.00 36.63
            546 CA PRO 278
    ATOM
15
                               40.242 2.639 10.783 1.00 32.95
           547 CB PRO 278
    ATOM
                               41.668 2.419 10.343 1.00 35.75
    ATOM
           548 CG PRO 278
    ATOM
            549 C PRO 278
                              40.532 4.681 12.306 1.00 38.60
            550 O PRO 278
                              39.653 5.017 13.104 1.00 37.67
    ATOM
                              41.831 4.758 12.586 1.00 37.05
            551 N ALA 279
    ATOM
20
                               42.315 5.248 13.877 1.00 33.18
            552 CA ALA 279
    ATOM
                               43.836 5.135 13.949 1.00 30.56
    ATOM
            553 CB ALA 279
           554 C ALA 279
                              41.890 6.692 14.077 1.00 33.47
     ATOM
                              41.403 7.060 15.151 1.00 33.74
           555 O ALA 279
     ATOM
                              42.067 7.517 13.041 1.00 29.96
            556 N ILE 280
    ATOM
25
                              41.687 8.921 13.121 1.00 25.94
     ATOM
            557 CA ILE 280
            558 CB ILE 280
                              42.155 9.716 11.871 1.00 26.95
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           559 CG2 ILE 280
                               41.643 11.168 11.923 1.00 15.40
     MOTA
                               43.686 9.702 11.798 1.00 26.73
           560 CG1 ILE 280
     ATOM
                               44.255 10.378 10.550 1.00 34.31
           561 CD1 ILE 280
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     ATOM
                              40.181 9.074 13.251 1.00 31.39
     ATOM
           562 C ILE 280
            563 O ILE 280
                              39.696 9.943 13.973 1.00 35.69
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                               39.428 8.226 12.552 1.00 30.90
            564 N THR 281
     ATOM
                               37.982 8.318 12.592 1.00 33.49
            565 CA THR 281
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                               37.321 7.451 11.478 1.00 37.18
            566 CB THR 281
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     ATOM
                                37.760 6.091 11.592 1.00 46.48
            567 OG1 THR 281
     ATOM
                                37.703 7.972 10.114 1.00 32.85
           568 CG2 THR 281
     ATOM
                               37.435 7.926 13.968 1.00 29.94
     ATOM 569 C THR 281
                               36.428 8.473 14.408 1.00 25.55
            570 O THR 281
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                               38.103 6.997 14.641 1.00 32.70
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           571 N ARG 282
                                37.676 6.585 15.975 1.00 34.27
            572 CA ARG 282
     ATOM
                                38.511 5.411 16.479 1.00 33.78
     ATOM
            573 CB ARG 282
                                38.259 4.111 15.743 1.00 45.15
            574 CG ARG 282
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                                39.017 2.976 16.404 1.00 58.24
     ATOM
            575 CD ARG 282
                                38.763 1.679 15.776 1.00 68.41
            576 NE ARG 282
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     ATOM
     ATOM
            577 CZ ARG 282
                                39.141 1.344 14.546 1.00 72.31
             578 NH1 ARG 282
                                39.802 2.213 13.791 1.00 77.89
     ATOM
                                38.864 0.139 14.066 1.00 69.25
     ATOM
            579 NH2 ARG 282
                               37.789 7.764 16.942 1.00 34.81
            580 C ARG 282
     ATOM
                               37.006 7.886 17.884 1.00 36.03
     ATOM 581 O ARG 282
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    ATOM
            583 CA VAL 283
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    ATOM
           584 CB VAL 283
                               40.298 10.524 17.224 1.00 29.00
    ATOM
           585 CG1 VAL 283
                               40.448 11.777 18.076 1.00 28.64
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    ATOM 586 CG2 VAL 283
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                              37.801 10.787 17.292 1.00 32.50
           587 C VAL 283
    ATOM
    ATOM 588 O VAL 283
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                              37.403 10.945 16.028 1.00 30.96
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    ATOM 590 CA VAL 284
                               36.293 11.838 15.694 1.00 29.14
    ATOM 591 CB VAL 284
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                               34.990 12.985 13.868 1.00 24.21
    ATOM 592 CG1 VAL 284
    ATOM 593 CG2 VAL 284
                               37.450 12.565 13:554 1.00 30.51
                              34.995 11.260 16.258 1.00 28.89
    ATOM 594 C VAL 284
    ATOM 595 O VAL 284
                              34.146 12.005 16.743 1.00 27.29
    ATOM 596 N ASP 285
                              34.845 9.937 16.208 1.00 28.76
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                              33.639 9.307 16.738 1.00 35.32
    ATOM 597 CA ASP 285
                              33.627 7.792 16.459 1.00 33.29
    ATOM 598 CB ASP 285
    ATOM 599 CG ASP 285
                              33.523 7.471 14.971 1.00 38.15
    ATOM 600 OD1 ASP 285
                               32.729 8.139 14.276 1.00 34.70
    ATOM 601 OD2 ASP 285
                               34.209 6.532 14.504 1.00 34.43
20
                              33.531 9.553 18.248 1.00 36.70
    ATOM 602 C ASP 285
                              32.431 9.685 18.786 1.00 37.96
    ATOM 603 O ASP 285
    ATOM 604 N PHE 286
                              34.679 9.624 18.916 1.00 35.96
                               34.736 9.869 20.349 1.00 37.10
    ATOM 605 CA PHE 286
    ATOM 606 CB PHE 286
                               36.187 9.777 20.845 1.00 37.97
25
                               36.377 10.219 22.283 1.00 36.50
    ATOM 607 CG PHE 286
    ATOM 608 CD1 PHE 286
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    ATOM 609 CD2 PHE 286
                               37.100 11.381 22.575 1.00 33.83
                               35.966 9.917 24.685 1.00 39.55
    ATOM 610 CE1 PHE 286
                               37,265 11.831 23.911 1.00 38.08
    ATOM 611 CE2 PHE 286
30
                              36.696 11.092 24.972 1.00 34.44
    ATOM 612 CZ PHE 286
                              34.179 11.249 20.665 1.00 36.83
    ATOM 613 C PHE 286
    ATOM 614 O PHE 286
                              33.292 11.401 21.518 1.00 35.61
                              34.696 12.255 19.968 1.00 37.33
    ATOM 615 N ALA 287
                               34.266 13.631 20.171 1.00 36.34
    ATOM 616 CA ALA 287
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                               35.118 14.565 19.325 1.00 36.40
    ATOM 617 CB ALA 287
                              32.785 13.840 19.861 1.00 38.76
    ATOM 618 C ALA 287
    ATOM 619 O ALA 287
                              32.121 14.641 20.525 1.00 41.98
    ATOM 620 N LYS 288
                              32.267 13.130 18.862 1.00 38.28
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     ATOM 621 CA LYS 288
                               30.856 13.268 18.499 1.00 45.26
     ATOM 622 CB LYS 288
                               30.541 12.534 17.188 1.00 48.35
                               31.159 13.158 15.951 1.00 51.43
    ATOM 623 CG LYS 288
     ATOM 624 CD LYS 288
                               30.556 12.589 14.665 1.00 60.23
                               30.848 11.107 14.479 1.00 62.81
     ATOM 625 CE LYS 288
     ATOM 626 NZ LYS 288
                               32.312 10.852 14.392 1.00 64.69
45
                              29.913 12.763 19.586 1.00 43.31
     ATOM 627 C LYS 288
     ATOM 628 O LYS 288
                              28.791 13.253 19.707 1.00 45.66
                              30,367 11,789 20,371 1,00 41,70
     ATOM 629 N LYS 289
     ATOM 630 CA LYS 289
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     ATOM 631 CB LYS 289
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29.912 8.853 20.591 1.00 39.53
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            632 CG LYS 289
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            633 CD LYS 289
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                               30.454 6.539 19.807 1.00 45.74
            634 CE LYS 289
    ATOM
            635 NZ LYS 289
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                              29.585 12.076 22.721 1.00 41.50
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                              29.030 11.676 23.742 1.00 39.77
            637 O LYS 289
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            638 N LEU 290
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                               30.307 14.143 23.811 1.00 39.33
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           639 CA LEU 290
           640 CB LEU 290
                               31.757 14.590 24.075 1.00 36.14
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            641 CG LEU 290
                               32.815 13.526 24.401 1.00 34.81
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                                34.155 14.200 24.558 1.00 29.07
           642 CD1 LEU 290
    ATOM
    ATOM 643 CD2 LEU 290
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           644 C LEU 290
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                              29.828 16.196 22.655 1.00 42.00
           645 O LEU 290
    ATOM
                              28.279 15.500 24.137 1.00 40.27
    ATOM 646 N PRO 291
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    ATOM 647 CD PRO 291
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    ATOM 649 CB PRO 291
                               26.327 16.447 24.997 1.00 35.88
    ATOM 650 CG PRO 291
                               26.230 14.932 25.071 1.00 34.19
                              28.010 18.006 23.910 1.00 40.05
    ATOM 651 C PRO 291
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                              27.663 18.857 23.089 1.00 41.33
           652 O PRO 291
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    ATOM 653 N MET 292
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    ATOM 654 CA MET 292
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                               30.635 19.521 26.059 1.00 43.28
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    ATOM
                               30.050 19.286 27.428 1.00 50.35
           656 CG MET 292
    ATOM
25
    ATOM 657 SD MET 292
                               31.329 19.157 28.679 1.00 51.17
            658 CE MET 292
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                               30.311 19.869 23.629 1.00 41.05
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                               30.341 21.024 23.210 1.00 39.66
     ATOM 660 O MET 292
     ATOM 661 N PHE 293
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    ATOM 662 CA PHE 293
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    ATOM 663 CB PHE 293
                               32.300 17.772 21.335 1.00 40.98
                               33.117 17.902 20.070 1.00 42.78
    ATOM 664 CG PHE 293
     ATOM 665 CD1 PHE 293
                                34.272 18.692 20.046 1.00 44.40
    ATOM 666 CD2 PHE 293
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                               35.051 18.823 18.865 1.00 39.83
     ATOM 667 CE1 PHE 293
                              33.483 17.348 17.710 1.00 46.21
     ATOM 668 CE2 PHE 293
            669 CZ PHE 293
                               34.654 18.147 17.693 1.00 45.18
     ATOM
                              30.653 19.492 20.624 1.00 45.54
     ATOM 670 C PHE 293
                              30.985 20.377 19.829 1.00 42.01
     ATOM 671 O PHE 293
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                              29.468 18.895 20.579 1.00 47.05
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                               28.545 19.200 19.512 1.00 50.15
     ATOM 673 CA CYS 294
     ATOM 674 CB CYS 294
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     ATOM 675 SG CYS 294
                               27.680 16.529 19.352 1.00 51.50
                              28.062 20.636 19.582 1.00 51.38
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45
           677 O CYS 294
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     ATOM 678 N GLU 295
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     ATOM 679 CA GLU 295
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     ATOM 681 CG GLU 295
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24.871 22.731 22.785 1.00 78.49
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            683 OE1 GLU 295
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            684 OE2 GLU 295
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                               28.170 24.777 20.537 1.00 49.82
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            687 N LEU 296
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            698 CB PRO 297
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            704 CB CYS 298
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            705 SG CYS 298
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                               33,269 23,797 12,974 1.00 48.51
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     ATOM
            707 O CYS 298
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            710 CB GLU 299
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            711 CG GLU 299
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            713 OE1 GLU 299
     ATOM
            714 OE2 GLU 299
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            718 CA ASP 300
            719 CB ASP 300
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             721 OD1 ASP 300
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            722 OD2 ASP 300
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            723 C ASP 300
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            724 O ASP 300
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             726 CA GLN 301
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	ATOM	785 N CYS 309	44.053 15.247 17.907 1.00 28.46
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	ATOM	788 SG CYS 309	43.761 12.613 14.819 1.00 35.20
	ATOM	789 C CYS 309	45.301 13.071 17.524 1.00 27.72
	ATOM	790 O CYS 309	45.135 11.907 17.913 1.00 27.69
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	ATOM	802 CG GLU 311	47.610 15.999 21.331 1.00 26.00
	ATOM	803 CD GLU 311	47.292 17.271 22.084 1.00 23.95
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	ATOM	805 OE2 GLU 311	48.150 18.181 22.088 1.00 26.51
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	ATOM-	807 O GLU 311	47.152 11.552 22.807 1.00 29.67
	ATOM	808 N ILE 312	45.547 12.086 21.326 1.00 26.82
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	ATOM	810 CB ILE 312	43.194 11.296 21.304 1.00 23.35
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	ATOM	812 CG1 ILE 312	42.690 12.534 22.062 1.00 20.88
	ATOM	813 CD1 ILE 312	41.244 12.961 21.755 1.00 18.15
	ATOM	814 C ILE 312	45.116 9.665 21.132 1.00 27.91
	ATOM	815 O ILE 312	45.064 8.628 21.804 1.00 28.96
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	ATOM	818 CB MET 313	46.386 8.662 17.771 1.00 36.89
	ATOM	819 CG MET 313	45.186 8.938 16.861 1.00 37.95
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	ATOM	823 O MET 313	47.351 6.690 20.219 1.00 28.61
	ATOM	824 N SER 314	48.202 8.776 20.318 1.00 24.88
	ATOM	825 CA SER 314	49.416 8.352 21.011 1.00 27.98
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	ATOM	827 OG SER 314	49.912 10.560 21.911 1.00 43.44
	ATOM	828 C SER 314	49.082 7.818 22.402 1.00 22.30
	ATOM	829 O SER 314	49.737 6.895 22.892 1.00 24.18
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	ATOM	833 CG LEU 315	45.863 8.355 26.228 1.00 20.39
	ATOM	834 CD1 LEU 315	46.872 8.076 27.362 1.00 18.92
	ATOM	835 CD2 LEU 315	44.848 9.401 26.655 1.00 12.93
5	ATOM	836 C LEU 315	47.070 6.518 24.222 1.00 24.53
-	ATOM	837 O LEU 315	47.394 5.615 24.992 1.00 26.32
	ATOM	838 N ARG 316	46.212 6.338 23.220 1.00 28.18
	ATOM	839 CA ARG 316	45.595 5.041 22.978 1.00 27.54
	ATOM	840 CB ARG 316	44.575 5.155 21.848 1.00 27.39
10	ATOM	841 CG ARG 316	43.340 5.929 22.253 1.00 22.00
••	ATOM	842 CD ARG 316	42.291 5.902 21.172 1.00 18.78
	ATOM	843 NE ARG 316	40.975 6.205 21.719 1.00 26.57
	ATOM	844 CZ ARG 316	39.852 6.224 21.014 1.00 30.81
	ATOM	845 NH1 ARG 316	39.878 5.972 19.711 1.00 33.71
15	ATOM	846 NH2 ARG 316	38.692 6.471 21.613 1.00 33.13
	ATOM	847 C ARG 316	46.612 3.949 22.682 1.00 28.09
	ATOM	848 O ARG 316	46.399 2.790 23.027 1.00 32.41
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	ATOM	852 C ALA 317	49.591 3.115 23.002 1.00 28.35
	ATOM	853 O ALA 317	49.968 1.979 23.312 1.00 32.10
	ATOM	854 N ALA 318	49.863 4.197 23.727 1.00 29.12
	ATOM	855 CA ALA 318	50,655 4.123 24.953 1.00 27.50
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	ATOM	857 C ALA 318	50.053 3.215 26.013 1.00 28.10
	ATOM	858 O ALA 318	50.783 2.491 26.684 1.00 28.18
	ATOM	859 N VAL 319	48.730 3.245 26.165 1.00 29.16
	ATOM	860 CA VAL 319	48.082 2.414 27.176 1.00 35.24
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	ATOM	862 CG1 VAL 319	46.759 4.324 28.136 1.00 29.96
	ATOM	863 CG2 VAL 319	45.773 2.936 26.322 1.00 31.70
	ATOM	864 C VAL 319	47.970 0.955 26.764 1.00 40.01
	ATOM	865 O VAL 319	47.448 0.129 27.515 1.00 42.70
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	ATOM	868 CB ARG 320	47.764 -0.751 23.674 1.00 37.26
	ATOM	869 CG ARG 320	46.258 -0.655 23.720 1.00 43.12
	ATOM	870 CD ARG 320	45.712 -0.368 22.339 1.00 50.79
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	ATOM	873 NH1 ARG 320	44.119 0.713 20.300 1.00 49.08
	ATOM	874 NH2 ARG 320	42.206 -0.058 21.326 1.00 59.59
	ATOM	875 C ARG 320	49.852 -1.247 24.930 1.00 42.14
45	ATOM	876 O ARG 320	50.162 -2.055 24.051 1.00 46.30
	ATOM	877 N TYR 321	50.712 -0.772 25.822 1.00 42.04
	ATOM	878 CA TYR 321	52.098 -1.202 25.852 1.00 42.70
	ATOM	879 CB TYR 321	52.971 -0.133 26.529 1.00 38.01
	ATOM	880 CG TYR 321	54.416 -0.579 26.734 1.00 37.94
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                               55.016 -2.926 16.783 1.00 42.35
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                               54.876 -1.687 15.877 1.00 42.41
    ATOM 987 CB VAL 336
                               53.963 -2.004 14.707 1.00 42.00
    ATOM 988 CG1 VAL 336
                               54.313 -0.506 16.676 1.00 40.32
    ATOM 989 CG2 VAL 336
    ATOM 990 C VAL 336
                              56.023 -2.608 17.883 1.00 45.33
                              55.650 -2.309 19.019 1.00 47.42
    ATOM 991 O VAL 336
10
                              57.310 -2.678 17.541 1.00 41.60
    ATOM 992 N THR 337
    ATOM 993 CA THR 337
                               58.357 -2.381 18.508 1.00 39.69
                               59.608 -3.259 18.296 1.00 41.35
    ATOM 994 CB THR 337
                               60.168 -2.985 17.007 1.00 49.35
    ATOM 995 OG1 THR 337
                               59.253 -4.734 18.392 1.00 40.38
15
    ATOM 996 CG2 THR 337
    ATOM 997 C THR 337
                              58.777 -0.924 18.367 1.00 37.88
    ATOM 998 O THR 337
                              58.312 -0.218 17.473 1.00 34.06
    ATOM 999 N ARG 338
                              59.655 -0.489 19.268 1.00 37.61
    ATOM 1000 CA ARG 338
                                60.171 0.876 19.268 1.00 38.68
                                61.177 1.041 20.424 1.00 35.95
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    ATOM 1001 CB ARG 338
    ATOM 1002 CG ARG 338
                                61.804 2.434 20.570 1.00 38.83
                                62.791 2.462 21.749 1.00 35.88
    ATOM 1003 CD ARG 338
                                62.114 2.277 23.035 1.00 37.42
    ATOM 1004 NE ARG 338
                               61.858 3.256 23.902 1.00 30.20
    ATOM 1005 CZ ARG 338
    ATOM 1006 NH1 ARG 338
                                62.224 4.501 23.636 1.00 27.98
25
                                61.213 2.992 25.025 1.00 27.40
    ATOM 1007 NH2 ARG 338
                               60.843 1.158 17.925 1.00 38.09
    ATOM 1008 C ARG 338
                               60.529 2.142 17.251 1.00 34.12
    .ATOM 1009 O ARG 338
                               61.755 0.267 17.535 1.00 41.25
    ATOM 1010 N GLY 339
    ATOM 1011 CA GLY 339
                               62.475 0.416 16.282 1.00 41.35
30
                               61.594 0.463 15.046 1.00 41.23
    ATOM 1012 C GLY 339
    ATOM 1013 O GLY 339
                               61.811 1.288 14.159 1.00 38.30
     ATOM 1014 N GLN 340
                               60.594 -0.414 14.982 1.00 38.58
    ATOM 1015 CA GLN 340
                                59.704 -0.449 13.826 1.00 40.79
                                58.757 -1.651 13.911 1.00 40.82
     ATOM 1016 CB GLN 340
35
                                59.450 -2.995 13.944 1.00 41.10
     ATOM 1017 CG GLN 340
    ATOM 1018 CD GLN 340
                                58.468 -4.144 13.890 1.00 48.84
    ATOM 1019 OE1 GLN 340
                                57.529 -4.208 14.679 1.00 50.53
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                                58.685 -5.068 12.959 1.00 54.25
                               58.884 0.822 13.679 1.00 41.50
     ATOM 1021 C GLN 340
40
                               58.725 1.342 12.576 1.00 42.72
     ATOM 1022 O GLN 340
                               58.360 1.324 14.795 1.00 42.00
     ATOM 1023 N LEU 341
     ATOM 1024 CA LEU 341
                               57.546 2.532 14.775 1.00 38.10
     ATOM 1025 CB LEU 341
                               56.868 2.740 16.133 1.00 36.66
                                55.886 3.914 16.267 1.00 39.94
     ATOM 1026 CG LEU 341
45
                                54.711 3.741 15.311 1.00 34.98
     ATOM 1027 CD1 LEU 341
     ATOM 1028 CD2 LEU 341
                                55.389 3.989 17.700 1.00 40.95
                               58.404 3.743 14.423 1.00 36.37
     ATOM 1029 C LEU 341
                               57.980 4.620 13.668 1.00 37.89
     ATOM 1030 O LEU 341
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     ATOM 1031 N LYS 342
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	ATOM	1032 CA LYS 342	60.542 4.872 14.723 1.00 35.17
	ATOM	1033 CB LYS 342	61.801 4.687 15.582 1.00 34.97
	ATOM	1034 CG LYS 342	62.764 5.863 15.519 1.00 40.00
	ATOM	1035 CD LYS 342	63.868 5.739 16.555 1.00 34.48
5	ATOM	1036 CE LYS 342	64.709 7.001 16.596 1.00 37.54
	ATOM	1037 NZ LYS 342	65.716 6.972 17.689 1.00 42.32
	ATOM	1038 C LYS 342	60.928 4.970 13.235 1.00 38.29
	ATOM	1039 O LYS 342	60.621 5.963 12.569 1.00 36.23
	ATOM	1040 N ASN 343	61.585 3.932 12.721 1.00 39.25
10	ATOM	1041 CA ASN 343	62.014 3.903 11.328 1.00 40.19
	ATOM	1042 CB ASN 343	62.808 2.627 11.050 1.00 37.96
	ATOM	1043 CG ASN 343	63.937 2.429 12.027 1.00 39.22
	ATOM	1044 OD1 ASN 343	64.648 3.376 12.374 1.00 42.37
	ATOM	1045 ND2 ASN 343	64.125 1.197 12.471 1.00 42.19
15	ATOM	1046 C ASN 343	60.831 3.997 10.368 1.00 40.12
	ATOM	1047 O ASN 343	60.991 4.371 9.208 1.00 36.01
	ATOM	1048 N GLY 344	59.645 3.665 10.868 1.00 40.95
	ATOM	1049 CA GLY 344	58.439 3.721 10.057 1.00 39.25
	ATOM	1050 C GLY 344	57.947 5.131 9.772 1.00 38.26
20	ATOM	1051 O GLY 344	56.971 5.308 9.044 1.00 35.69
	ATOM	1052 N GLY 345	58.604 6.135 10.359 1.00 35.89
	ATOM	1053 CA GLY 345	58.212 7.510 10.110 1.00 34.00
	ATOM	1054 C GLY 345	58.050 8.444 11.300 1.00 38.64
	ATOM	1055 O GLY 345	57.902 9.652 11.116 1.00 38.14
25	ATOM	1056 N LEU 346	58.085 7.912 12.520 1.00 39.52
	ATOM	1057 CA LEU 346	57.904 8.761 13.692 1.00 36.05
	ATOM	1058 CB LEU 346	57.039 8.048 14.738 1.00 35.72
	ATOM	1059 CG LEU 346	55.561 7.864 14.371 1.00 34.89
	ATOM	1060 CD1 LEU 346	54.850 7.132 15.494 1.00 44.09
30	ATOM	1061 CD2 LEU 346	54.903 9.213 14.146 1.00 34.84
	ATOM	1062 C LEU 346	59.189 9.264 14.339 1.00 33.52
	ATOM	1063 O LEU 346	59.171 10.257 15.066 1.00 35.58
	ATOM	1064 N GLY 347	60.299 8.595 14.067 1.00 30.47
	ATOM	1065 CA GLY 347	61.559 9.017 14.661 1.00 33.01
35	ATOM	1066 C GLY 347	61.504 9.069 16.182 1.00 30.72
	ATOM	1067 O GLY 347	60.967 8.160 16.812 1.00 30.89
	ATOM		62.051 10.132 16.765 1.00 31.30
		1069 CA VAL 348	
	ATOM		
40	ATOM		62.071 12.841 18.146 1.00 20.19
	ATOM		63.080 11.651 20.118 1.00 24.77
	ATOM		60.683 10.273 18.855 1.00 33.84
	ATOM		
	ATOM		
45	ATOM		
	ATOM		
		1078 CG1 VAL 349	55.837 10.678 17.838 1.00 33.68
		1079 CG2 VAL 349	
		1080 C VAL 349	
50	ATOM	1081 O VAL 349	57.133 8.932 19.980 1.00 33.73

	4 TO 3 4	1082 N SER 350	58.551 8.081 18.444 1.00 32.81
	ATOM ATOM	1082 N SER 350	58.335 6.704 18.853 1.00 30.10
	ATOM	1084 CB SER 350	59.041 5.746 17.904 1.00 24.95
,	ATOM	1084 CB SER 350	58.943 4.417 18.387 1.00 23.16
_		1086 C SER 350	58.863 6.486 20.266 1.00 31.59
5	ATOM	1080 C SER 350	58.207 5.845 21.086 1.00 37.62
	ATOM	1088 N ASP 351	60.055 7.007 20.546 1.00 28.60
	ATOM	1089 CA ASP 351	60.652 6.863 21.867 1.00 29.82
	ATOM	1090 CB ASP 351	62.048 7.491 21.919 1.00 27.49
10	ATOM	1091 CG ASP 351	63.030 6.806 21.000 1.00 30.22
10	ATOM	1092 OD1 ASP 351	63.411 7.412 19.974 1.00 32.61
	ATOM	1093 OD2 ASP 351	63.422 5.661 21.301 1.00 30.02
	ATOM		59.785 7.548 22.913 1.00 30.63
	ATOM		59.632 7.055 24.027 1.00 29.54
1.5	ATOM		59.222 8.692 22.537 1.00 25.33
15	ATOM	1096 N ALA 352 1097 CA ALA 352	58.390 9.464 23.432 1.00 28.59
	ATOM	1098 CB ALA 352	58.011 10.798 22.788 1.00 20.95
	ATOM	-	57.136 8.695 23.831 1.00 29.69
	ATOM		56.711 8.753 24.982 1.00 30.36
20	ATOM		56.557 7.979 22.876 1.00 27.63
20	ATOM	1101 N ILE 353 1102 CA ILE 353	55.345 7.227 23.129 1.00 27.55
	ATOM	1102 CA ILE 353.	54.611 6.925 21.805 1.00 28.04
	ATOM	1104 CG2 ILE 353	53.329 6.111 22.065 1.00 23.68
	ATOM	1104 CG2 ILE 353	54.269 8.251 21.119 1.00 27.33
25	ATOM	1106 CD1 ILE 353	53.637 8.105 19.734 1.00 26.23
25	ATOM	1107 C ILE 353	55.631 5.943 23.901 1.00 30.88
	ATOM ATOM	1107 C ILE 353	54.880 5.597 24.814 1.00 31.22
	ATOM	1109 N PHE 354	56.710 5.240 23.549 1.00 29.86
	ATOM	1110 CA PHE 354	57.056 4.022 24.275 1.00 31.08
30	ATOM	1111 CB PHE 354	58.227 3.274 23.619 1.00 28.80
30	ATOM	1112 CG PHE 354	57.799 2.322 22.523 1.00 28.80
	ATOM	1112 CO 111E 354	57.330 2.804 21.292 1.00 30.96
	ATOM	1113 CD111E 354	57.811 0.939 22.749 1.00 29.45
	ATOM	1115 CE1 PHE 354	56.864 1.909 20.281 1.00 27.12
35	ATOM	1116 CE2 PHE 354	57.354 0.026 21.761 1.00 25.19
33	ATOM	1110 CE211E 354	56.879 0.518 20.521 1.00 28.09
		1117 CZ THE 354	57.398 4.349 25.721 1.00 29.17
	ATOM		
	ATOM		
40	ATOM		58.508 5.873 27.262 1.00 25.34
40	ATOM		59.434 7.083 27.180 1.00 21.41
	ATOM		60.846 6.708 26.769 1.00 32.08
	ATOM		
	ATOM		
45	ATOM		57.254 6.211 28.062 1.00 27.86
43	ATOM		57.167 5.916 29.252 1.00 32.42
	ATOM		56.276 6.821 27.401 1.00 26.84
	ATOM		55.031 7.164 28.066 1.00 28.66
		1130 CB LEU 356	54.112 7.953 27.131 1.00 25.37
50		1130 CB LEU 356	52.787 8.427 27.742 1.00 27.61
50	ATOM	1131 CG LEO 330	J2.701 G.747 Z1.772 1.00 Z1.01

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53.056 9.452 28.842 1.00 25.43
    ATOM 1132 CD1 LEU 356
                                51.924 9.057 26.667 1.00 27.49
    ATOM 1133 CD2 LEU 356
                              54.334 5.875 28.473 1.00 30.44
    ATOM 1134 C LEU 356
    ATOM 1135 O LEU 356
                              53.873 5.743 29.601 1.00 31.55
                               54.266 4.928 27.536 1.00 32.69
    ATOM 1136 N GLY 357
                               53.621 3.652 27.787 1.00 29.87
    ATOM 1137 CA GLY 357
    ATOM 1138 C GLY 357
                               54,239 2.884 28.939 1.00 33.12
    ATOM 1139 O GLY 357
                               53,524 2.268 29.732 1.00 29.41
                               55.570 2.911 29.026 1.00 33.31
    ATOM 1140 N MET 358
                                56.277 2.217 30.100 1.00 35.87
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    ATOM 1141 CA MET 358
    ATOM 1142 CB MET 358
                               57.794 2.265 29.871 1.00 34.56
    ATOM 1143 CG MET 358
                                58.265 1.608 28.576 1.00 46.43
    ATOM 1144 SD MET 358
                               60.073 1.600 28.351 1.00 42.13
    ATOM 1145 CE MET 358
                               60.429 3.306 28.411 1.00 44.29
15
    ATOM 1146 C MET 358
                               55.948 2.884 31.434 1.00 33.26
    ATOM 1147 O MET 358
                               55.802 2.222 32.453 1.00 36.39
    ATOM 1148 N SER 359
                              55.825 4.202 31.398 1.00 33.31
                               55.533 4.998 32.580 1.00 34.39
    ATOM 1149 CA SER 359
                               55.859 6.463 32.303 1.00 30.84
    ATOM 1150 CB SER 359
    ATOM 1151 OG SER 359
                               55.487 7.265 33.404 1.00 47.14
20
                              54.094 4.897 33.072 1.00 36.43
    ATOM 1152 C SER 359
    ATOM 1153 O SER 359
                              53.833 5.073 34.260 1.00 35.46
    ATOM 1154 N LEU 360
                              53.165 4.617 32.156 1.00 36.74
                               51.750 4.519 32.493 1.00 35.44
    ATOM 1155 CA LEU 360
    ATOM 1156 CB LEU 360
                               50.889 4.817 31.263 1.00 34.16
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    ATOM 1157 CG LEU 360
                               50.896 6.263 30.751 1.00 34.59
                                50.031 6.353 29.513 1.00 33.53
    ATOM 1158 CD1 LEU 360
                                50.376 7.211 31.836 1.00 31.69
    ATOM 1159 CD2 LEU 360
    ATOM 1160 C LEU 360
                              51.324 3.192 33.088 1.00 38.72
                              50.185 3.058 33.546 1.00 38.29
    ATOM 1161 O LEU 360
30
    ATOM 1162 N SER 361
                              52.227 2.214 33.080 1.00 40.96
    ATOM 1163 CA SER 361
                               51.938 0.897 33.636 1.00 45.67
    ATOM 1164 CB SER 361
                               53.131 -0.044 33.436 1.00 46.45
    ATOM 1165 OG SER 361
                              53,362 -0.296 32.061 1.00 51.81
                              51.628 1.004 35.124 1.00 44.49
    ATOM 1166 C SER 361
35
    ATOM 1167 O SER 361
                              50.724 0.337 35.630 1.00 46.67
    ATOM 1168 N SER 362
                              52.385 1.858 35.809 1.00 41.44
    ATOM 1169 CA SER 362
                               52.231 2.081 37.245 1.00 42.13
                               53.431 2.876 37.779 1.00 42.61
    ATOM 1170 CB SER 362
    ATOM 1171 OG SER 362
                               54.647 2.215 37.492 1.00 51.87
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    ATOM 1172 C SER 362
                              50.951 2.832 37.610 1.00 38.41
    ATOM 1173 O SER 362
                              50.444 2.700 38.722 1.00 38.01
    ATOM 1174 N PHE 363
                              50.443 3.631 36.672 1.00 34.55
                               49.232 4.404 36.906 1.00 32.96
    ATOM 1175 CA PHE 363
45
    ATOM 1176 CB PHE 363
                               49.109 5.518 35.859 1.00 31.99
    ATOM 1177 CG PHE 363
                               50.093 6.659 36.058 1.00 29.97
    ATOM 1178 CD1 PHE 363
                                49.667 7.872 36.594 1.00 30.61
                                51.445 6.501 35.731 1.00 32.02
    ATOM 1179 CD2 PHE 363
    ATOM 1180 CE1 PHE 363
                                50.579 8.940 36.803 1.00 33.67
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    ATOM 1181 CE2 PHE 363
                               52.376 7.552 35.934 1.00 30.91
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ATOM 1182 CZ PHE 363 51.938 8.777 36.473 1.00 29.33 ATOM 1183 C PHE 363 47.973 3.554 36.916 1.00 30.52 46.971 3.947 37.491 1.00 32.19 ATOM 1184 O PHE 363 48.036 2.384 36.283 1.00 33.51 ATOM 1185 N ASN 364 46.894 1.471 36.216 1.00 38.03 ATOM 1186 CA ASN 364 ATOM 1187 CB ASN 364 46.754 0.711 37.539 1.00 42.32 47.824 -0.361 37.713 1.00 53.11 ATOM 1188 CG ASN 364 47.815 -1.370 37.012 1.00 59.51 ATOM 1189 OD1 ASN 364 48.751 -0.138 38.639 1.00 55.95 ATOM 1190 ND2 ASN 364 ATOM 1191 C ASN 364 45.574 2.161 35.871 1.00 31.89 10 44.587 2.027 36.588 1.00 30.28 ATOM 1192 O ASN 364 45,561 2.883 34,751 1.00 27.62 ATOM 1193 N LEU 365 44.365 3.606 34.317 1.00 29.36 ATOM 1194 CA LEU 365 ATOM 1195 CB LEU 365 44.738 4.627 33.240 1.00 27.54 45.826 5.659 33.576 1.00 38.91 ATOM 1196 CG LEU 365 15 46.115 6.499 32.338 1.00 34.47 ATOM 1197 CD1 LEU 365 45.394 6.546 34.743 1.00 34.24 ATOM 1198 CD2 LEU 365 ATOM 1199 C LEU 365 43.264 2.691 33.774 1.00 26.23 ATOM 1200 O LEU 365 43.546 1.648 33.197 1.00 27.06 42.011 3.074 33.991 1.00 25.23 20 ATOM 1201 N ASP 366 ATOM 1202 CA ASP 366 40.892 2.307 33.462 1.00 26.07 39.832 2.008 34.538 1.00 29.68 ATOM 1203 CB ASP 366 39.337 3.253 35.261 1.00 35.74 ATOM 1204 CG ASP 366 ATOM 1205 OD1 ASP 366 39.438 4.371 34.717 1.00 36.78 38.803 3.100 36.378 1.00 41.23 25 ATOM 1206 OD2 ASP 366 40.274 3.100 32.305 1.00 27.70 ATOM 1207 C ASP 366 40.748 4.191 31.975 1.00 31.94 ATOM 1208 O ASP 366 ATOM 1209 N ASP 367 39.223 2.564 31.693 1.00 29.18 38.594 3.233 30.560 1.00 32.72 ATOM 1210 CA ASP 367 30 37.428 2.395 30.018 1.00 38.04 ATOM 1211 CB ASP 367 37.855 0.995 29.606 1.00 42.43 ATOM 1212 CG ASP 367 38.913 0.852 28.956 1.00 35.95 ATOM 1213 OD1 ASP 367 37.115 0.034 29.917 1.00 51.42 ATOM 1214 OD2 ASP 367 38.093 4.631 30.881 1.00 33.71 ATOM 1215 C ASP 367 ATOM 1216 O ASP 367 38.059 5.506 30.013 1.00 38.30 35 ATOM 1217 N THR 368 37.705 4.852 32.132 1.00 31.06 37.199 6.155 32.543 1.00 26.28 ATOM 1218 CA THR 368 ATOM 1219 CB THR 368 36.537 6.066 33.922 1.00 27.30 ATOM 1220 OG1 THR 368 35.461 5.127 33.861 1.00 33.42 36.003 7.423 34.355 1.00 25.16 40 ATOM 1221 CG2 THR 368 38.303 7.194 32.593 1.00 21.13 ATOM 1222 C THR 368 ATOM 1223 O THR 368 38.133 8.314 32.104 1.00 23.17 39.431 6.816 33.179 1.00 21.32 ATOM 1224 N GLU 369 40.565 7.720 33.317 1.00 28.00 ATOM 1225 CA GLU 369 45 ATOM 1226 CB GLU 369 41.582 7.107 34.277 1.00 32.79 ATOM 1227 CG GLU 369 40.944 6.804 35.619 1.00 36.29 41.834 6.026 36.546 1.00 41.03 ATOM 1228 CD GLU 369 42.361 4.967 36.123 1.00 42.05 ATOM 1229 OE1 GLU 369 ATOM 1230 OE2 GLU 369 41.986 6.458 37.705 1.00 42.03 50 ATOM 1231 C GLU 369 41.201 8.047 31.970 1.00 25.57

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41.626 9.175 31.741 1.00 20.56
    ATOM 1232 O GLU 369
                               41.249 7.055 31.080 1.00 25.39
    ATOM 1233 N VAL 370
                                41.794 7.278 29.745 1.00 25.99
    ATOM 1234 CA VAL 370
                               42.005 5.936 28.977 1.00 26.15
    ATOM 1235 CB VAL 370
    ATOM 1236 CG1 VAL 370
                                42.450 6.216 27.539 1.00 27.65
                                43.056 5.086 29.685 1.00 17.70
    ATOM 1237 CG2 VAL 370
                               40.814 8.164 28.966 1.00 26.49
    ATOM 1238 C VAL 370
    ATOM 1239 O VAL 370
                               41.226 9.038 28.202 1.00 28.16
                               39.514 7.950 29.184 1.00 21.01
    ATOM 1240 N ALA 371
                               38.486 8.730 28.510 1.00 19.57
    ATOM 1241 CA ALA 371
    ATOM 1242 CB ALA 371
                               37.116 8.136 28.783 1.00 18.62
                               38.512 10.191 28.947 1.00 23.48
    ATOM 1243 C ALA 371
                               38.500 11.103 28.111 1.00 32.67
    ATOM 1244 O ALA 371
                               38.540 10.414 30.256 1.00 22.89
    ATOM 1245 N LEU 372
    ATOM 1246 CA LEU 372
                               38.560 11.772 30.806 1.00 23.28
15
                               38.517 11.709 32.343 1.00 27.76
    ATOM 1247 CB LEU 372
                               37.155 11.306 32.924 1.00 21.18
    ATOM 1248 CG LEU 372
                                37.289 10.891 34.381 1.00 27.64
    ATOM 1249 CD1 LEU 372
                                36.197 12.480 32.763 1.00 20.90
    ATOM 1250 CD2 LEU 372
    ATOM 1251 C LEU 372
                               39.804 12.505 30.357 1.00 21.34
20
                               39.779 13.708 30.086 1.00 23.16
    ATOM 1252 O LEU 372
                               40.896 11.761 30.276 1.00 24.42
    ATOM 1253 N LEU 373
                                42.177 12.302 29.855 1.00 23.78
    ATOM 1254 CA LEU 373
                               43,222 11.205 30.007 1.00 22.18
     ATOM 1255 CB LEU 373
                                44.724 11.456 30.036 1.00 31.52
25
     ATOM 1256 CG LEU 373
                                45.099 12.565 31.001 1.00 31.93
    ATOM 1257 CD1 LEU 373
                                45.382 10.152 30.460 1.00 30.24
     ATOM 1258 CD2 LEU 373
                               42.025 12.757 28.399 1.00 25.69
     ATOM 1259 C LEU 373
                               42.469 13.842 28.025 1.00 30.13
     ATOM 1260 O LEU 373
     ATOM 1261 N GLN 374
                               41.370 11.934 27.587 1.00 26.24
30
                                41.151 12.269 26.184 1.00 21.60
     ATOM 1262 CA GLN 374
                                40.501 11.091 25.444 1.00 24.57
     ATOM 1263 CB GLN 374
                                41.428 9.900 25.234 1.00 21.02
     ATOM 1264 CG GLN 374
                                40.762 8.744 24.501 1.00 22.86
     ATOM 1265 CD GLN 374
                                41.407 7.754 24.174 1.00 24.07
     ATOM 1266 OEI GLN 374
35
                                39.466 8.865 24.249 1.00 25.59
     ATOM 1267 NE2 GLN 374
                               40.267 13.498 26.070 1.00 20.66
     ATOM 1268 C GLN 374
                               40.518 14.366 25.242 1.00 24.47
     ATOM 1269 O GLN 374
                               39.237 13.579 26.902 1.00 16.26
     ATOM 1270 N ALA 375
                                38.337 14.727 26.870 1.00 17.16
     ATOM 1271 CA ALA 375
40
                                37.156 14.491 27.803 1.00 19.53
     ATOM 1272 CB ALA 375
                               39.056 16.024 27.252 1.00 25.13
     ATOM 1273 C ALA 375
     ATOM 1274 O ALA 375
                               38.722 17.100 26.750 1.00 23.81
                               40.036 15.926 28.156 1.00 24.57
     ATOM 1275 N VAL 376
                                40.796 17.101 28.568 1.00 25.80
     ATOM 1276 CA VAL 376
45
                                41.711 16.792 29.814 1.00 26.48
     ATOM 1277 CB VAL 376
                                42.625 17.971 30.102 1.00 23.20
     ATOM 1278 CG1 VAL 376
                                40.845 16.521 31.044 1.00 19.08
     ATOM 1279 CG2 VAL 376
                               41.653 17.580 27.396 1.00 25.69
     ATOM 1280 C VAL 376
     ATOM 1281 O VAL 376
                               41.775 18.780 27.151 1.00 27.87
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42.249 16.637 26.666 1.00 23.09
    ATOM 1282 N LEU 377
                                43.071 16.982 25.513 1.00 22.86
    ATOM 1283 CA LEU 377
                                43.748 15.730 24.962 1.00 18.50
    ATOM 1284 CB LEU 377
                                44.814 15.096 25.867 1.00 22.65
    ATOM 1285 CG LEU 377
                                45.144 13.708 25.374 1.00 16.70
    ATOM 1286 CD1 LEU 377
                                46.070 15.987 25.901 1.00 19.58
    ATOM 1287 CD2 LEU 377
    ATOM 1288 C LEU 377
                               42.197 17.634 24.430 1.00 26.14
                               42.579 18.638 23.830 1.00 20.62
    ATOM 1289 O LEU 377
                               41.016 17.057 24.208 1.00 28.99
    ATOM 1290 N LEU 378
    ATOM 1291 CA LEU 378
                                40.076 17.578 23.218 1.00 28.87
    ATOM 1292 CB LEU 378
                                38.814 16.710 23.182 1.00 26.89
    ATOM 1293 CG LEU 378
                                37.637 17.167 22.311 1.00 28.83
                                38.053 17.273 20.840 1.00 27.97
    ATOM 1294 CD1 LEU 378
                                36.496 16.175 22.478 1.00 27.69
    ATOM 1295 CD2 LEU 378
                               39.693 19.025 23.504 1.00 31.09
    ATOM 1296 C LEU 378
15
    ATOM 1297 O LEU 378
                               39.812 19.883 22.629 1.00 31.77
                               39.247 19.297 24.729 1.00 31.44
    ATOM 1298 N MET 379
    ATOM 1299 CA MET 379
                                38.841 20.649 25.104 1.00 32.62
    ATOM 1300 CB MET 379
                                37.876 20.603 26.293 1.00 31.45
    ATOM 1301 CG MET 379
                                36.586 19.855 26.010 1.00 38.75
20
    ATOM 1302 SD MET 379
                                35.646 20.541 24.601 1.00 41.27
                                34.231 19.443 24.609 1.00 35.68
    ATOM 1303 CE MET 379
                               39.980 21.613 25.421 1.00 33.72
    ATOM 1304 C MET 379
                               39.940 22.297 26.446 1.00 36.29
    ATOM 1305 O MET 379
                               40.981 21.676 24.543 1.00 34.49
25
     ATOM 1306 N SER 380
                                42.116 22.585 24.721 1.00 33.97
     ATOM 1307 CA SER 380
                                43.371 22.025 24.061 1.00 31.24
    ATOM 1308 CB SER 380
                                43.771 20.814 24.674 1.00 39.42
     ATOM 1309 OG SER 380
                               41.772 23.926 24.088 1.00 39.69
     ATOM 1310 C SER 380
                               41.787 24.069 22.864 1.00 44.64
     ATOM 1311 O SER 380
30
     ATOM 1312 N SER 381
                               41.472 24.907 24.927 1.00 41.04
                                41.090 26.234 24.462 1.00 44.91
     ATOM 1313 CA SER 381
                                40.406 27.004 25.594 1.00 44.50
     ATOM 1314 CB SER 381
     ATOM 1315 OG SER 381
                                41.294 27.177 26.678 1.00 45.42
                               42.231 27.084 23.921 1.00 44.59
     ATOM 1316 C SER 381
35
                               42.012 28.227 23.516 1.00 49.32
     ATOM 1317 O SER 381
                               43.440 26.541 23.896 1.00 43.75
     ATOM 1318 N ASP 382
                                44.571 27.315 23.407 1.00 43.93
     ATOM 1319 CA ASP 382
     ATOM 1320 CB ASP 382
                                45.817 27.047 24.257 1.00 48.39
                                46.319 25.632 24.113 1.00 53.23
     ATOM 1321 CG ASP 382
40
                                45.590 24.702 24.517 1.00 56.97
     ATOM 1322 OD1 ASP 382
     ATOM 1323 OD2 ASP 382
                                 47.440 25.449 23.584 1.00 58.91
                               44.900 27.026 21.955 1.00 41.09
     ATOM 1324 C ASP 382
                               45.912 27.502 21.446 1.00 40.93
     ATOM 1325 O ASP 382
                                44.068 26.236 21.287 1.00 42.63
45
     ATOM 1326 N ARG 383
     ATOM 1327 CA ARG 383
                                44.316 25.937 19.876 1.00 43.32
     ATOM 1328 CB ARG 383
                                43.289 24.935 19.331 1.00 42.31
                                43.174 23.619 20.095 1.00 40.83
     ATOM 1329 CG ARG 383.
                                 44.478 22.835 20.139 1.00 38.09
     ATOM 1330 CD ARG 383
     ATOM 1331 NE ARG 383
                                44.271 21.542 20.787 1.00 37.33
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45.235 20.690 21.115 1.00 38.35
    ATOM 1332 CZ ARG 383
                                 46.505 20.972 20.850 1.00 33.70
    ATOM 1333 NH1 ARG 383
    ATOM 1334 NH2 ARG 383
                                 44.922 19.545 21.704 1.00 35.46
    ATOM 1335 C ARG 383
                               44.166 27.256 19.127 1.00 44.96
                               43.214 28.006 19.361 1.00 45.60
    ATOM 1336 O ARG 383
                               45.112 27.574 18.230 1.00 45.33
    ATOM 1337 N PRO 384
    ATOM 1338 CD PRO 384
                                46.330 26.852 17.836 1.00 46.85
    ATOM 1339 CA PRO 384
                                45.024 28.830 17.484 1.00 47.37
    ATOM 1340 CB PRO 384
                               46.323 28.823 16.672 1.00 46.90
                               47.257 27.998 17.552 1.00 46.41
    ATOM 1341 CG PRO 384
10
    ATOM 1342 C PRO 384
                               43.788 28.910 16.590 1.00 48.29
    ATOM 1343 O PRO 384
                               43.394 27.927 15.960 1.00 48.34
                               43.176 30.090 16.552 1.00 49.88
    ATOM 1344 N GLY 385
                                42.013 30.290 15.712 1.00 50.35
    ATOM 1345 CA GLY 385
    ATOM 1346 C GLY 385
                               40.669 29.958 16.324 1.00 50.70
15
                               39.639 30.201 15.697 1.00 53.48
    ATOM 1347 O GLY 385
    ATOM 1348 N LEU 386
                               40.663 29.404 17.529 1.00 49.04
    ATOM 1349 CA LEU 386
                               39.405 29.057 18.182 1.00 50.53
    ATOM 1350 CB LEU 386
                               39.655 28.433 19.558 1.00 45.17
                                40.245 27.019 19.544 1.00 48.26
20
    ATOM 1351 CG LEU 386
    ATOM 1352 CD1 LEU 386
                                40.502 26.564 20.970 1.00 41.68
    ATOM 1353 CD2 LEU 386
                                39.285 26.065 18.836 1.00 38.40
    ATOM 1354 C LEU 386
                               38.495 30.268 18.319 1.00 52.13
                               38.955 31.395 18.476 1.00 53.67
    ATOM 1355 O LEU 386
25
    ATOM 1356 N ALA 387
                               37.193 30.020 18.261 1.00 53.42
    ATOM 1357 CA ALA 387
                                36.225 31.093 18.354 1.00 56.01
    ATOM 1358 CB ALA 387
                                35.221 30.976 17.202 1.00 56.47
                               35.482 31.144 19.681 1.00 55.52
    ATOM 1359 C ALA 387
    ATOM 1360 O ALA 387
                               35.491 32.171 20.358 1.00 53.75
                               34.854 30.038 20.065 1.00 56.03
    ATOM 1361 N CYS 388
30
                               34.072 30.036 21.312 1.00 59.57
    ATOM 1362 CA CYS 388
    ATOM 1363 CB CYS 388
                               32.724 29.351 21.089 1.00 59.23
    ATOM 1364 SG CYS 388
                               31.314 30.363 21.641 1.00 58.64
    ATOM 1365 C CYS 388
                               34.846 29.289 22.398 1.00 62.18
    ATOM 1366 O CYS 388
                               34.458 28.190 22.790 1.00 67.88
35
    ATOM 1367 N VAL 389
                               35,955 29,950 22,760 1.00 60.78
                                37.005 29.583 23.713 1.00 57.70
    ATOM 1368 CA VAL 389
                                38,202 30.580 23.565 1.00 57.09
    ATOM 1369 CB VAL 389
    ATOM 1370 CG1 VAL 389
                                39.351 30.194 24.494 1.00 59.03
    ATOM 1371 CG2 VAL 389
                                38.671 30.618 22.124 1.00 53.98
40
    ATOM 1372 C VAL 389
                               36.661 29.515 25.195 1.00 57.77
    ATOM 1373 O VAL 389
                               36.943 28.513 25.851 1.00 60.94
                               36.102 30.594 25.732 1.00 52.68
    ATOM 1374 N GLU 390
    ATOM 1375 CA GLU 390
                                35.738 30.636 27.138 1.00 48.41
    ATOM 1376 CB GLU 390
                                35.001 31.928 27.451 1.00 45.19
45
    ATOM 1377 C GLU 390
                               34.868 29.439 27.459 1.00 47.63
                               34,986 28.837 28.529 1.00 51.95
    ATOM 1378 O GLU 390
    ATOM 1379 N ARG 391
                               34.002 29.082 26.517 1.00 47.11
                                33.099 27.950 26.699 1.00 51.64
    ATOM 1380 CA ARG 391
                                32.050 27.930 25.588 1.00 54.22
    ATOM 1381 CB ARG 391
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30.830 27.094 25.915 1.00 64.20
    ATOM 1382 CG ARG 391
    ATOM 1383 CD ARG 391
                                29.867 27.074 24.748 1.00 73.80
                                28.533 26.622 25.128 1.00 79.76
    ATOM 1384 NE ARG 391
                                27.714 27.298 25.929 1.00 84.27
    ATOM 1385 CZ ARG 391
                                28.090 28.465 26.439 1.00 85.28
    ATOM 1386 NH1 ARG 391
                                 26.515 26.809 26.217 1.00 86.84
    ATOM 1387 NH2 ARG 391
    ATOM 1388 C ARG 391
                               33.890 26.644 26.684 1.00 48.18
    ATOM 1389 O ARG 391
                               33.504 25.671 27.330 1.00 49.57
    ATOM 1390 N ILE 392
                              34.987 26.625 25.936 1.00 45.01
    ATOM 1391 CA ILE 392
                               35.835 25.440 25.858 1.00 48.77
10
                               36.854 25.565 24.692 1.00 46.45
    ATOM 1392 CB ILE 392
    ATOM 1393 CG2 ILE 392
                               37.798 24.370 24.679 1.00 42.35
                               36.086 25.664 23.367 1.00 49.69
    ATOM 1394 CG1 ILE 392
                               36.950 25.897 22.136 1.00 51.09
    ATOM 1395 CD1 ILE 392
                              36,570 25.246 27.192 1.00 50.90
    ATOM 1396 C ILE 392
15
    ATOM 1397 O ILE 392
                              36.731 24.118 27.657 1.00 52.21
                               36.999 26.346 27.811 1.00 50.43
    ATOM 1398 N GLU 393
    ATOM 1399 CA GLU 393
                                37.673 26.267 29.101 1.00 50.30
                                38.202 27.638 29.531 1.00 53.97
    ATOM 1400 CB GLU 393
                                39.322 28.168 28.658 1.00 62.18
    ATOM 1401 CG GLU 393
20
                                39.911 29.478 29.168 1.00 67.69
    ATOM 1402 CD GLU 393
                                40.869 29.977 28.537 1.00 66.42
    ATOM 1403 OE1 GLU 393
                                39.423 30.009 30.191 1.00 70.64
    ATOM 1404 OE2 GLU 393
    ATOM 1405 C GLU 393
                               36.686 25.765 30.145 1.00 49.31
    ATOM 1406 O GLU 393
                               37.018 24.923 30.980 1.00 49.53
25
                               35.468 26.286 30.090 1.00 46.07
    ATOM 1407 N LYS 394
                               34.428 25.893 31.022 1.00 45.76
    ATOM 1408 CA LYS 394
    ATOM 1409 CB LYS 394
                               33.147 26.666 30.727 1.00 43.85
                               34.188 24.391 30.909 1.00 46.69
    ATOM 1410 C LYS 394
                               33.982 23.699 31.911 1.00 49.13
    ATOM 1411 O LYS 394
30
                               34.223 23.887 29.679 1.00 46.57
    ATOM 1412 N TYR 395
                                34.014 22.467 29.427 1.00 43.33
    ATOM 1413 CA TYR 395
    ATOM 1414 CB TYR 395.
                                33.818 22.211 27.929 1.00 48.44
                                32.493 22.710 27.335 1.00 53.83
    ATOM 1415 CG TYR 395
    ATOM 1416 CD1 TYR 395
                                32.302 22.727 25.947 1.00 56.43
35
                                31.078 23.148 25.374 1.00 59.73
    ATOM 1417 CE1 TYR 395
                                31.434 23.132 28.153 1.00 56.47
    ATOM 1418 CD2 TYR 395
    ATOM 1419 CE2 TYR 395
                                30.198 23.559 27.592 1.00 62.60
                                30.037 23.562 26.200 1.00 63.18
    ATOM 1420 CZ TYR 395
                                28.834 23.962 25.635 1.00 64.46
    ATOM 1421 OH TYR 395
40
                               35.189 21.635 29.938 1.00 37.30
    ATOM 1422 C TYR 395
                               34.993 20.599 30.564 1.00 34.10
    ATOM 1423 O TYR 395
                               36.408 22.091 29.671 1.00 31.92
     ATOM 1424 N GLN 396
     ATOM 1425 CA GLN 396
                                37.584 21.363 30.120 1.00 34.81
                                38.861 21.987 29.560 1.00 32.64
     ATOM 1426 CB GLN 396
45
    ATOM 1427 CG GLN 396
                                40.114 21.183 29.882 1.00 29.57
                                41.370 21.827 29.352 1.00 29.46
     ATOM 1428 CD GLN 396
     ATOM 1429 OEI GLN 396
                                41.648 22.982 29.649 1.00 34.65
     ATOM 1430 NE2 GLN 396
                                42.139 21.088 28.570 1.00 27.21
                               37.647 21.342 31.647 1.00 37.13
     ATOM 1431 C GLN 396
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	ATOM	1432 O GLN 396	37.939 20.302 32.236 1.00 37.36
	ATOM	1433 N ASP 397	37.371 22.484 32.284 1.00 38.61
	ATOM	1434 CA ASP 397	37.393 22.555 33.742 1.00 40.37
	ATOM	1435 CB ASP 397	37.099 23.973 34.240 1.00 40.51
5	ATOM	1436 CG ASP 397	38.130 24.974 33.772 1.00 43.77
	ATOM	1437 OD1 ASP 397	39.330 24.632 33.775 1.00 46.50
	ATOM	1438 OD2 ASP 397	37.750 26.109 33.422 1.00 51.34
	ATOM	1439 C ASP 397	36.352 21.601 34.295 1.00 38.62
	ATOM	1440 O ASP 397	36.515 21.034 35.372 1.00 39.20
10	ATOM	1441 N SER 398	35.282 21.423 33.540 1.00 37.84
	ATOM	1442 CA SER 398	34.221 20.524 33.942 1.00 37.80
	ATOM	1443 CB SER 398	33.039 20.669 32.984 1.00 34.28
	ATOM	1444 OG SER 398	31.981 19.815 33.360 1.00 46.60
	ATOM	1445 C SER 398	34.752 19.082 33.939 1.00 38.41
15	ATOM	1446 O SER 398	34.372 18.274 34.787 1.00 39.98
	ATOM	1447 N PHE 399	35.630 18.772 32.987 1.00 34.82
	ATOM	1448 CA PHE 399	36.213 17.433 32.885 1.00 35.96
	ATOM	1449 CB PHE 399	36.809 17.181 31.493 1.00 35.75
	ATOM	1450 CG PHE 399	35.775 16.936 30.419 1.00 39.30
20	ATOM	1451 CD1 PHE 399	35.640 17.826 29.344 1.00 39.86
	ATOM	1452 CD2 PHE 399	34.936 15.819 30.487 1.00 36.81
	ATOM	1453 CE1 PHE 399	34.674 17.607 28.330 1.00 41.25
	ATOM	1454 CE2 PHE 399	33.962 15.577 29.488 1.00 43.61
	ATOM	1455 CZ PHE 399	33.829 16.480 28.402 1.00 40.34
25	ATOM	1456 C PHE 399	37.306 17.217 33.921 1.00 33.48
	ATOM	1457 O PHE 399	37.406 16.139 34.512 1.00 26.86
	ATOM	1458 N LEU 400	38.132 18.239 34.118 1.00 31.47
	ATOM	1459 CA LEU 400	39.213 18.162 35.086 1.00 37.41
	ATOM	1460 CB LEU 400	40.051 19.441 35.038 1.00 34.24
30	ATOM	1461 CG LEU 400	40.934 19.574 33.788 1.00 35.10
50	ATOM	1462 CD1 LEU 400	41.469 20.991 33.651 1.00 26.60
	ATOM	1463 CD2 LEU 400	42.077 18.569 33.884 1.00 29.44
	ATOM	1464 C LEU 400	38.666 17.931 36.491 1.00 38.84
	ATOM	1465 O LEU 400	39.137 17.049 37.205 1.00 40.38
35	ATOM	1466 N LEU 401	37.654 18.703 36.870 1.00 42.79
	ATOM	1467 CA LEU 401	37.056 18.584 38.197 1.00 43.48
		1468 CB LEU 401	35.997 19.675 38.406 1.00 44.73
		1469 CG LEU 401	35.322 19.737 39.779 1.00 51.39
	ATOM		36.359 20.002 40.866 1.00 50.11
40		1471 CD2 LEU 401	34.273 20.834 39.778 1.00 49.30
70		1472 C LEU 401	36.433 17.215 38.409 1.00 41.62
	ATOM		36.563 16.622 39.482 1.00 45.14
	ATOM		35.744 16.712 37.389 1.00 37.92
	ATOM		35.115 15.402 37.484 1.00 29.90
45		1476 CB ALA 402	34.196 15.187 36.297 1.00 30.70
7.7	ATOM		36.203 14.336 37.508 1.00 28.88
	ATOM		36.083 13.322 38.188 1.00 32.14
	ATOM		37.274 14.588 36.764 1.00 32.14
	ATOM		38.402 13.656 36.661 1.00 29.90
50	ATOM	1480 CA PHE 403	39.396 14.178 35.605 1.00 27.03
20	AIOM	1401 CD PRE 403	37.370 14.170 33.003 1.00 27.03

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ATOM 1482 CG PHE 403
                                40.434 13.146 35.140 1.00 26.97
                                41.362 13.509 34.149 1.00 25.55
     ATOM 1483 CD1 PHE 403
                                40.475 11.841 35.664 1.00 19.75
     ATOM 1484 CD2 PHE 403
     ATOM 1485 CE1 PHE 403
                                42.331 12.588 33.679 1.00 27.90
                                41.441 10.899 35.206 1.00 22.56
     ATOM 1486 CE2 PHE 403
                                42.371 11.273 34.210 1.00 22.24
     ATOM 1487 CZ PHE 403
                               39.081 13.523 38.023 1.00 28.82
     ATOM 1488 C PHE 403
                               39.313 12.413 38.495 1.00 26.00
     ATOM 1489 O PHE 403
                               39.405 14.652 38.652 1.00 30.25
     ATOM 1490 N GLU 404
10
     ATOM 1491 CA GLU 404
                                40.039 14.627 39.966 1.00 34.03
                                40.264 16.046 40.497 1.00 39.45
     ATOM 1492 CB GLU 404
                                40.987 16.076 41.839 1.00 47.68
     ATOM 1493 CG GLU 404
     ATOM 1494 CD GLU 404
                                41.062 17.465 42.446 1.00 54.02
                                41.607 18.380 41.796 1.00 57.27
     ATOM 1495 OE1 GLU 404
     ATOM 1496 OE2 GLU 404
                                40.573 17.638 43.585 1.00 63.85
15
                               39.164 13.860 40.960 1.00 36.01
     ATOM 1497 C GLU 404
     ATOM 1498 O GLU 404
                               39.661 12.997 41.701 1.00 38.64
     ATOM 1499 N HIS 405
                              37.870 14.168 40.975 1.00 29.56
     ATOM 1500 CA HIS 405
                               36.949 13.508 41.892 1.00 31.69
     ATOM 1501 CB HIS 405
                               35.534 14.077 41.757 1.00 33.75
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     ATOM 1502 CG HIS 405
                               35.401 15.498 42.213 1.00 34.75
                                36.308 16.361 42.730 1.00 34.58
     ATOM 1503 CD2 HIS 405
     ATOM 1504 ND1 HIS 405
                                34.207 16.187 42.146 1.00 32.43
     ATOM 1505 CE1 HIS 405
                               34.385 17.414 42.598 1.00 36.15
                                35.650 17.549 42.960 1.00 39.84
     ATOM 1506 NE2 HIS 405
25
                              36.904 12.013 41.673 1.00 34.21
     ATOM 1507 C HIS 405
                              36.700 11.247 42.624 1.00 37.06
     ATOM 1508 O HIS 405
     ATOM 1509 N TYR 406
                               37.081 11.594 40.419 1.00 30.83
     ATOM 1510 CA TYR 406
                                37.059 10.173 40.093 1.00 28.85
                                37.018 9.959 38.575 1.00 31.48
     ATOM 1511 CB TYR 406
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     ATOM 1512 CG TYR 406
                                36.879 8.490 38.181 1.00 23.49
                                35.683 7.798 38.397 1.00 19.42
     ATOM 1513 CD1 TYR 406
                                35.556 6.427 38.059 1.00 23.80
     ATOM 1514 CE1 TYR 406
     ATOM 1515 CD2 TYR 406
                                37.950 7.794 37.624 1.00 21.81
                                37.838 6.421 37.278 1.00 24.64
     ATOM 1516 CE2 TYR 406
35
     ATOM 1517 CZ TYR 406
                                36.639 5.753 37.503 1.00 21.56
                                36.537 4.404 37.186 1.00 24.96
     ATOM 1518 OH TYR 406
     ATOM 1519 C TYR 406
                               38.318 9.526 40.638 1.00 24.24
     ATOM 1520 O TYR 406
                               38.308 8.375 41.050 1.00 27.08
                              39.407 10.278 40.617 1.00 25.76
40
     ATOM 1521 N ILE 407
     ATOM 1522 CA ILE 407
                               40.688 9.799 41.105 1.00 33.75
                               41.815 10.822 40.796 1.00 34.23
     ATOM 1523 CB ILE 407
     ATOM 1524 CG2 ILE 407
                                43.121 10.400 41.435 1.00 32.46
                                41.959 10.972 39.275 1.00 43.30
     ATOM 1525 CG1 ILE 407
                               42.267 9.677 38.523 1.00 40.40
45
     ATOM 1526 CD1 ILE 407
                              40.620 9.556 42.613 1.00 39.03
     ATOM 1527 C ILE 407
                              41.192 8.583 43.107 1.00 35.18
     ATOM 1528 O ILE 407
     ATOM 1529 N ASN 408
                               39.916 10.440 43.335 1.00 37.25
                                39.778 10.292 44.777 1.00 37.01
     ATOM 1530 CA ASN 408
                                39.099 11.514 45.400 1.00 32.27
50
     ATOM 1531 CB ASN 408
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ATOM 1532 CG ASN 408
                               39.887 12.790 45.187 1.00 33.56
                                41.118 12.785 45.225 1.00 31.99
    ATOM 1533 OD1 ASN 408
                                39.182 13.903 44.996 1.00 31.23
    ATOM 1534 ND2 ASN 408
                               38.961 9.046 45.055 1.00 38.14
    ATOM 1535 C ASN 408
    ATOM 1536 O ASN 408
                               39.303 8.243 45.920 1.00 42.16
    ATOM 1537 N TYR 409
                               37.874 8.894 44.303 1.00 35.62
                               37.002 7.733 44.412 1.00 35.91
    ATOM 1538 CA TYR 409
                               35.929 7.804 43.323 1.00 34.41
    ATOM 1539 CB TYR 409
                               35.196 6.495 43.066 1.00 38.73
    ATOM 1540 CG TYR 409
    ATOM 1541 CD1 TYR 409
                                34.266 5.982 43.980 1.00 41.34
10
                                33.600 4.745 43.741 1.00 47.16
    ATOM 1542 CE1 TYR 409
                                35.461 5.752 41.907 1.00 46.20
    ATOM 1543 CD2 TYR 409
    ATOM 1544 CE2 TYR 409
                                34.814 4.518 41.651 1.00 50.74
                               33.891 4.023 42.573 1.00 50.88
    ATOM 1545 CZ TYR 409
    ATOM 1546 OH TYR 409
                               33.262 2.816 42.302 1.00 53.14
15
                               37.827 6.459 44.240 1.00 38.16
    ATOM 1547 C TYR 409
    ATOM 1548 O TYR 409
                               37.806 5.561 45.082 1.00 41.83
                               38.551 6.399 43.125 1.00 42.25
    ATOM 1549 N ARG 410
    ATOM 1550 CA ARG 410
                               39.410 5.272 42.765 1.00 42.83
                               40.029 5.540 41.392 1.00 36.83
    ATOM 1551 CB ARG 410
20
                                39.055 5,397 40.249 1.00 34.32
    ATOM 1552 CG ARG 410
                                39.134 3.996 39.681 1.00 36.62
    ATOM 1553 CD ARG 410
    ATOM 1554 NE ARG 410
                                40.420 3.787 39.013 1.00 38.64
    ATOM 1555 CZ ARG 410
                               40.832 2.625 38.517 1.00 35.73
                                40.068 1.548 38.617 1.00 33.17
25
    ATOM 1556 NH1 ARG 410
                                42.006 2.544 37.916 1.00 32.70
    ATOM 1557 NH2 ARG 410
                               40.520 5.039 43.780 1.00 46.67
    ATOM 1558 C ARG 410
    ATOM 1559 O ARG 410
                               40.900 3.901 44.053 1.00 41.78
                              41.026 6.140 44.325 1.00 52.99
    ATOM 1560 N LYS 411
                               42.109 6.141 45.298 1.00 58.32
    ATOM 1561 CA LYS 411
30
                               41.565 5.956 46.731 1.00 64.99
    ATOM 1562 CB LYS 411
    ATOM 1563 CG LYS 411
                               40.660 4.763 46.977 1.00 70.48
                               40.034 4.866 48.364 1.00 77.18
    ATOM 1564 CD LYS 411
    ATOM 1565 CE LYS 411
                               39.053 3.732 48.625 1.00 84.30
                               38.392 3.865 49.958 1.00 86.48
    ATOM 1566 NZ LYS 411
35
    ATOM 1567 C LYS 411
                              43.238 5.163 45.000 1.00 56.66
                              43.329 4.075 45.575 1.00 55.47
    ATOM 1568 O LYS 411
                              44.091 5.582 44.070 1.00 54.67
    ATOM 1569 N HIS 412
                              45.266 4.823 43.657 1.00 48.67
    ATOM 1570 CA HIS 412
                              45.878 5.442 42.393 1.00 43.14
    ATOM 1571 CB HIS 412
                               45.073 5.218 41.156 1.00 41.36
    ATOM 1572 CG HIS 412
                               44.084 5.952 40.584 1.00 35.44
    ATOM 1573 CD2 HIS 412
    ATOM 1574 ND1 HIS 412
                               45.220 4.093 40.364 1.00 38.19
                               44.357 4.150 39.363 1.00 34.75
    ATOM 1575 CE1 HIS 412
    ATOM 1576 NE2 HIS 412
                               43.659 5.263 39.474 1.00 35.52
45
                              46.264 4.932 44.793 1.00 46.35
    ATOM 1577 C HIS 412
    ATOM 1578 O HIS 412
                              46.326 5.951 45.479 1.00 42.73
                              47.049 3.883 44.993 1.00 48.92
    ATOM 1579 N HIS 413
                              48.040 3.903 46.052 1.00 53.15
    ATOM 1580 CA HIS 413
                             48.148 2.515 46.688 1.00 55.27
50
    ATOM 1581 CB HIS 413
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46.843 2.015 47.238 1.00 58.77
    ATOM 1582 CG HIS 413
                               46.138 0.892 46.977 1.00 61.65
    ATOM 1583 CD2 HIS 413
    ATOM 1584 ND1 HIS 413
                               46.108 2.726 48.161 1.00 60.31
    ATOM 1585 CE1 HIS 413
                               45.003 2.061 48.445 1.00 63.01
    ATOM 1586 NE2 HIS 413
                               44.993 0.942 47.743 1.00 62.93
    ATOM 1587 C HIS 413
                              49.359 4.364 45.456 1.00 53.19
                              50.335 3.617 45.390 1.00 54.93
    ATOM 1588 O HIS 413
                               49.343 5.612 44.999 1.00 53.77
    ATOM 1589 N VAL 414
    ATOM 1590 CA VAL 414
                               50.487 6.282 44.389 1.00 51.06
    ATOM 1591 CB VAL 414
                               50.374 6.305 42.838 1.00 51.49
10
                               51.603 6.958 42.231 1.00 45.22
    ATOM 1592 CG1 VAL 414
    ATOM 1593 CG2 VAL 414
                                50.210 4.891 42.304 1.00 52.67
    ATOM 1594 C VAL 414
                               50.444 7.724 44.894 1.00 54.28
    ATOM 1595 O VAL 414
                               49.418 8.401 44.774 1.00 55.49
                               51.547 8.190 45.467 1.00 56.28
    ATOM 1596 N THR 415
15
    ATOM 1597 CA THR 415 51.610 9.550 45.986 1.00 57.83
    ATOM 1598 CB THR 415
                               52.874 9.756 46.858 1.00 59.64
    ATOM 1599 OG1 THR 415
                               52.922 11.115 47.311 1.00 66.69
    ATOM 1600 CG2 THR 415
                                54.137 9.436 46.067 1.00 59.42
    ATOM 1601 C THR 415
                              51.599 10.577 44.855 1.00 56.98
20
                              52.176 10.345 43.789 1.00 55.70
    ATOM 1602 O THR 415
    ATOM 1603 N HIS 416 50.936 11.707 45.093 1.00 57.44
    ATOM 1604 CA HIS 416 50.835 12.786 44.108 1.00 57.34
                             52,207 13.425 43.875 1.00 61.35
    ATOM 1605 CB HIS 416
    ATOM 1606 CG HIS 416 52.860 13.940 45.123 1.00 69.78
25
    ATOM 1607 CD2 HIS 416 54.049 13.633 45.695 1.00 71.42
    ATOM 1608 ND1 HIS 416 52.283 14.901 45.922 1.00 72.49
    ATOM 1609 CE1 HIS 416
                               53.087 15.165 46.938 1.00 75.50
                             54.165 14.410 46.819 1.00 73.91
    ATOM 1610 NE2 HIS 416
                              50.301 12.260 42.773 1.00 53.79
30
    ATOM 1611 C HIS 416
    ATOM 1612 O HIS 416
                              50.769 12.667 41.710 1.00 52.81
                              49.318 11.366 42.824 1.00 48.05
    ATOM 1613 N PHE 417
    ATOM 1614 CA PHE 417
                               48.769 10.784 41.610 1.00 47.99
    ATOM 1615 CB PHE 417
                               47.652 9.799 41.940 1.00 46.11
                               47.314 8.868 40.791 1.00 44.27
    ATOM 1616 CG PHE 417
35
                                48.155 7.796 40.481 1.00 41.79
    ATOM 1617 CD1 PHE 417
                                46.179 9.091 40.003 1.00 40.23
    ATOM 1618 CD2 PHE 417
                               47.872 6.936 39.386 1.00 44.30
    ATOM 1619 CE1 PHE 417
                               45.874 8.248 38.907 1.00 36.80
    ATOM 1620 CE2 PHE 417
    ATOM 1621 CZ PHE 417
                               46.725 7.167 38.595 1.00 40.69
40
                              48.227 11.824 40.625 1.00 46.69
    ATOM 1622 C PHE 417
                              48.551 11.787 39.436 1.00 43.35
    ATOM 1623 O PHE 417
                              47.410 12.746 41.124 1.00 45.14
    ATOM 1624 N TRP 418
    ATOM 1625 CA TRP 418
                               46.821 13.775 40.276 1.00 44.89
                               45.808 14.604 41.077 1.00 42.24
45
    ATOM 1626 CB TRP 418
                               45.096 15.646 40.259 1.00 47.11
    ATOM 1627 CG TRP 418
                                44.186 15.417 39.159 1.00 46.98
    ATOM 1628 CD2 TRP 418
                               43.786 16.678 38.676 1.00 48.94
    ATOM 1629 CE2 TRP 418
    ATOM 1630 CE3 TRP 418
                               43.676 14.261 38.548 1.00 45.23
    ATOM 1631 CD1 TRP 418
                               45.204 17.003 40.387 1.00 46.24
50
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44.425 17.637 39.448 1.00 50.63
    ATOM 1632 NE1 TRP 418
                                42.891 16.839 37.598 1.00 45.46
    ATOM 1633 CZ2 TRP 418
                                42.780 14.411 37.468 1.00 44.50
    ATOM 1634 CZ3 TRP 418
                                42,403 15,696 37,009 1,00 47,55
    ATOM 1635 CH2 TRP 418
                              47.862 14.676 39.598 1.00 43.88
    ATOM 1636 C TRP 418
                               47.834 14.842 38.383 1.00 43.17
    ATOM 1637 O TRP 418
    ATOM 1638 N PRO 419
                               48.788 15.281 40.369 1.00 43.55
                                49.006 15.290 41.826 1.00 41.52
    ATOM 1639 CD PRO 419
                                49.787 16.135 39.725 1.00 41.48
    ATOM 1640 CA PRO 419
                                50.626 16.627 40.912 1.00 39.21
    ATOM 1641 CB PRO 419
10
                                49.593 16.667 42.017 1.00 39.25
    ATOM 1642 CG PRO 419
                               50.616 15.363 38.701 1.00 36.28
    ATOM 1643 C PRO 419
                               50.940 15.882 37.638 1.00 37.08
    ATOM 1644 O PRO 419
                               50.959 14.124 39.033 1.00 35.96
    ATOM 1645 N LYS 420
                                51.742 13.281 38.132 1.00 40.82
15
    ATOM 1646 CA LYS 420
    ATOM 1647 CB LYS 420
                                52.094 11.945 38.792 1.00 40.78
                                53.086 12.046 39.933 1.00 48.62
    ATOM 1648 CG LYS 420
                                53.391 10.668 40.497 1.00 55.12
    ATOM 1649 CD LYS 420
                               54.395 10.741 41.635 1.00 53.26
    ATOM 1650 CE LYS 420
                                54.719 9.388 42.152 1.00 52.69
20
    ATOM 1651 NZ LYS 420
    ATOM 1652 C LYS 420
                               50,957 13.005 36.860 1.00 40.29
                               51.516 12.989 35.764 1.00 39.66
    ATOM 1653 O LYS 420
    ATOM 1654 N LEU 421
                               49.658 12.786 37.023 1.00 38.33
                                48.784 12.507 35.903 1.00 37.60
    ATOM 1655 CA LEU 421
    ATOM 1656 CB LEU 421
                                47.417 12.074 36.428 1.00 43.66
25
                                46.386 11.479 35.474 1.00 46.50
    ATOM 1657 CG LEU 421
                                46.946 10.253 34.770 1.00 45.15
    ATOM 1658 CD1 LEU 421
                                45.154 11.107 36.279 1.00 51.31
    ATOM 1659 CD2 LEU 421
                               48.661 13.747 35.014 1.00 39.59
    ATOM 1660 C LEU 421
    ATOM 1661 O LEU 421
                               48.599 13.638 33.791 1.00 40.66
30
                               48.642 14.928 35.623 1.00 39.57
    ATOM 1662 N LEU 422
                                48.545 16.170 34.867 1.00 38.63
    ATOM 1663 CA LEU 422
                                48.313 17.357 35.802 1.00 41.79
    ATOM 1664 CB LEU 422
    ATOM 1665 CG LEU 422
                                46.996 17.407 36.581 1.00 42.74
    ATOM 1666 CD1 LEU 422
                                47.010 18.606 37.515 1.00 42.89
35
                                45,823 17.494 35.628 1.00 39.27
     ATOM 1667 CD2 LEU 422
                               49.808 16.410 34.039 1.00 40.47
    ATOM 1668 C LEU 422
     ATOM 1669 O LEU 422
                               49.747 17.029 32.979 1.00 47.83
     ATOM 1670 N MET 423
                               50.949 15.936 34.519 1.00 34.27
    ATOM 1671 CA MET 423
                                52.187 16.103 33.774 1.00 35.25
40
                                53.403 15.716 34.622 1.00 32.56
     ATOM 1672 CB MET 423
     ATOM 1673 CG MET 423
                                53.675 16.654 35.774 1.00 40.70
                                55,226 16.278 36.597 1.00 47.65
     ATOM 1674 SD MET 423
                                54.920 14.601 37.163 1.00 47.16
     ATOM 1675 CE MET 423
                               52.164 15.254 32.502 1.00 35.13
     ATOM 1676 C MET 423
45
                               52.934 15.499 31.570 1.00 29.85
     ATOM 1677 O MET 423
                               51.285 14.252 32.482 1.00 31.56
     ATOM 1678 N LYS 424
                                51.152 13.384 31.316 1.00 32.29
     ATOM 1679 CA LYS 424
     ATOM 1680 CB LYS 424
                                50.373 12.115 31.681 1.00 30.56
     ATOM 1681 CG LYS 424
                                51.106 11.178 32.631 1.00 30.07
50
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52.248 10.482 31.938 1.00 33.22
    ATOM 1682 CD LYS 424
                               53.059 9.593 32.875 1.00 28.75
    ATOM 1683 CE LYS 424
                               53.868 10.383 33.833 1.00 31.01
    ATOM 1684 NZ LYS 424
    ATOM 1685 C LYS 424
                               50.435 14.150 30.197 1.00 29.26
                               50.719 13.944 29.030 1.00 30.22
    ATOM 1686 O LYS 424
                               49.514 15.036 30.573 1.00 23.53
    ATOM 1687 N VAL 425
    ATOM 1688 CA VAL 425
                               48.792 15.849 29.601 1.00 28.91
                                47.808 16.829 30.295 1.00 29.44
    ATOM 1689 CB VAL 425
    ATOM 1690 CG1 VAL 425
                                47.148 17.737 29.273 1.00 28.81
    ATOM 1691 CG2 VAL 425
                                46.744 16.049 31.057 1.00 31.22
10
                               49.822 16.669 28.831 1.00 32.03
    ATOM 1692 C VAL 425
    ATOM 1693 O VAL 425
                               49.771 16.769 27.605 1.00 31.95
                               50.763 17.247 29.570 1.00 33.61
    ATOM 1694 N THR 426
    ATOM 1695 CA THR 426
                               51.821 18.057 28.995 1.00 30.76
                               52.678 18.695 30.105 1.00 32.34
    ATOM 1696 CB THR 426
15
    ATOM 1697 OG1 THR 426
                               51.842 19.535 30.912 1.00 33.07
    ATOM 1698 CG2 THR 426
                                53.812 19.533 29.514 1.00 25.40
    ATOM 1699 C THR 426
                               52.712 17.225 28.086 1.00 32.53
                               53.113 17.686 27.014 1.00 35.19
    ATOM 1700 O THR 426
                               53.022 16.003 28.507 1.00 28.83
    ATOM 1701 N ASP 427
20
                               53.858 15.130 27.695 1.00 35.12
    ATOM 1702 CA ASP 427
    ATOM 1703 CB ASP 427
                               54.273 13.880 28.476 1.00 39.14
                               55.122 14.212 29.693 1.00 45.80
    ATOM 1704 CG ASP 427
                                56.052 15.034 29.556 1.00 41.97
    ATOM 1705 OD1 ASP 427
                                54.869 13.642 30.775 1.00 50.06
    ATOM 1706 OD2 ASP 427
25
    ATOM 1707 C ASP 427
                               53.124 14.726 26.422 1.00 33.94
                               53.737 14.617 25.362 1.00 38.02
    ATOM 1708 O ASP 427
                               51.818 14.512 26.529 1.00 27.15
    ATOM 1709 N LEU 428
                               51.013 14.148 25.373 1.00 29.99
    ATOM 1710 CA LEU 428
                                49.602 13.719 25.802 1.00 22.49
    ATOM 1711 CB LEU 428
30
                               49.541 12.285 26.359 1.00 25.54
    ATOM 1712 CG LEU 428
    ATOM 1713 CD1 LEU 428
                                48.210 12.021 27.037 1.00 20.60
                                49.785 11.303 25.224 1.00 17.24
    ATOM 1714 CD2 LEU 428
                               50.947 15.305 24.381 1.00 28.94
    ATOM 1715 C LEU 428
    ATOM 1716 O LEU 428
                               50.941 15.088 23.174 1.00 31.26
35
    ATOM 1717 N ARG 429
                               50.910 16.531 24.887 1.00 27.64
                                50.877 17.694 24.011 1.00 28.13
    ATOM 1718 CA ARG 429
                                50.584 18.969 24.800 1.00 29.59
    ATOM 1719 CB ARG 429
                                49.224 18.980 25.455 1.00 34.85
    ATOM 1720 CG ARG 429
    ATOM 1721 CD ARG 429
                                48.951 20.314 26.118 1.00 47.18
40
                                47.657 20.358 26.797 1.00 57.93
    ATOM 1722 NE ARG 429
    ATOM 1723 CZ ARG 429
                                46.473 20.193 26.200 1.00 63.62
                                 46.402 19.972 24.889 1.00 60.71
     ATOM 1724 NH1 ARG 429
    ATOM 1725 NH2 ARG 429
                                 45.356 20.257 26.919 1.00 62.38
                               52.229 17.819 23.304 1.00 29.81
     ATOM 1726 C ARG 429
                               52.294 18.209 22.143 1.00 30.81
     ATOM 1727 O ARG 429
                               53.305 17.482 24.008 1.00 29.64
     ATOM 1728 N MET 430
                                54.639 17.545 23.422 1.00 34.72
     ATOM 1729 CA MET 430
     ATOM 1730 CB MET 430
                                55.716 17.323 24.485 1.00 34.97
                                55.864 18.480 25.451 1.00 45.34
     ATOM 1731 CG MET 430
50
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ATOM 1732 SD MET 430
                                56.162 20.050 24.596 1.00 52.55
                                57.598 19.639 23.589 1.00 55.56
    ATOM 1733 CE MET 430
    ATOM 1734 C MET 430
                               54.778 16.500 22.325 1.00 34.01
                               55.440 16.733 21.318 1.00 37.29
    ATOM 1735 O MET 430
                              54.161 15.340 22.533 1.00 29.99
    ATOM 1736 N ILE 431
                               54.197 14.279 21.545 1.00 28.82
    ATOM 1737 CA ILE 431
                               53,523 12.984 22.095 1.00 27.39
    ATOM 1738 CB ILE 431
                               53.260 11.989 20.956 1.00 23.87
    ATOM 1739 CG2 ILE 431
                               54.414 12.386 23.201 1.00 25.56
    ATOM 1740 CG1 ILE 431
                               53.850 11.155 23.896 1.00 17.29
10
    ATOM 1741 CD1 ILE 431
    ATOM 1742 C ILE 431
                              53.450 14.785 20.301 1.00 29.49
    ATOM 1743 O ILE 431
                              53.908 14.603 19.174 1.00 24.19
                               52.311 15.435 20.524 1.00 25.25
    ATOM 1744 N GLY 432
                                51.542 15.971 19.419 1.00 30.38
    ATOM 1745 CA GLY 432
15
    ATOM 1746 C GLY 432
                               52,334 16.997 18.614 1.00 32.75
    ATOM 1747 O GLY 432
                               52.410 16.895 17.387 1.00 36.38
                               52.930 17.974 19.294 1.00 26.77
    ATOM 1748 N ALA 433
    ATOM 1749 CA ALA 433
                                53.711 19.012 18.625 1.00 26.48
                                54.182 20.047 19.631 1.00 19.90
    ATOM 1750 CB ALA 433
    ATOM 1751 C ALA 433
                               54.902 18.407 17.890 1.00 30.73
20
                               55.207 18.787 16.760 1.00 31.60
    ATOM 1752 O ALA 433
                               55.582 17.467 18.537 1.00 33.22
    ATOM 1753 N CYS 434
                                56.728 16.801 17.914 1.00 34.34
    ATOM 1754 CA CYS 434
                                57.339 15.808 18.895 1.00 35.20
    ATOM 1755 CB CYS 434
                               59.191 15.745 18.798 1.00 54.48
    ATOM 1756 SG CYS 434
25
                               56.313 16.052 16.636 1.00 34.09
    ATOM 1757 C CYS 434
                               57.095 15.937 15.679 1.00 34.89
    ATOM 1758 O CYS 434
                              55.088 15.545 16.642 1.00 34.30
    ATOM 1759 N HIS 435
                               54.570 14.818 15.501 1.00 35.44
    ATOM 1760 CA HIS 435
                               53.296 14.061 15.886 1.00 31.76
    ATOM 1761 CB HIS 435
30
                               52.587 13.469 14.715 1.00 32.03
    ATOM 1762 CG HIS 435
    ATOM 1763 CD2 HIS 435
                                52.735 12.277 14.092 1.00 28.61
                                51.665 14.177 13.970 1.00 28.48
    ATOM 1764 ND1 HIS 435
    ATOM 1765 CE1 HIS 435
                               51.284 13.453 12.941 1.00 33.27
                                51.920 12.284 12.985 1.00 31.57
    ATOM 1766 NE2 HIS 435
35
    ATOM 1767 C HIS 435
                              54.311 15.750 14.319 1.00 32.74
                              54.504 15.363 13.175 1.00 32.87
    ATOM 1768 O HIS 435
                               53.881 16.975 14.608 1.00 31.01
    ATOM 1769 N ALA 436
                                53.628 17.966 13.571 1.00 29.91
    ATOM 1770 CA ALA 436
                                53.221 19.290 14.197 1.00 21.23
    ATOM 1771 CB ALA 436
40
    ATOM 1772 C ALA 436
                               54.911 18.135 12.769 1.00 33.86
                               54.892 18.128 11.541 1.00 36.10
    ATOM 1773 O ALA 436
    ATOM 1774 N SER 437
                               56,030 18.266 13.483 1.00 35.19
                                57.344 18.426 12.871 1.00 33.03
    ATOM 1775 CA SER 437
                                58.389 18.720 13.941 1.00 35.31
45
    ATOM 1776 CB SER 437
     ATOM 1777 OG SER 437
                                59.681 18.782 13.373 1.00 44.99
    ATOM 1778 C SER 437
                               57.758 17.178 12.100 1.00 38.39
                               58.374 17.269 11.034 1.00 37.54
     ATOM 1779 O SER 437
                               57.427 16.012 12.642 1.00 37.32
     ATOM 1780 N ARG 438
    ATOM 1781 CA ARG 438
50
                               57.762 14.754 11.992 1.00 39.30
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57.517 13.572 12.941 1.00 42.97
    ATOM 1782 CB ARG 438
    ATOM 1783 CG ARG 438
                                58.542 13.436 14.059 1.00 41.72
                                59.926 13.212 13.484 1.00 45.23
    ATOM 1784 CD ARG 438
                                59.961 12.050 12.601 1.00 45.66
    ATOM 1785 NE ARG 438
                                60.935 11.804 11.731 1.00 49.71
    ATOM 1786 CZ ARG 438
                                61.961 12.641 11.627 1.00 50.91
    ATOM 1787 NH1 ARG 438
                                60.885 10.727 10.960 1.00 46.86
    ATOM 1788 NH2 ARG 438
    ATOM 1789 C ARG 438
                               56.939 14.565 10.725 1.00 42.37
                               57.311 13.794 9.841 1.00 40.58
    ATOM 1790 O ARG 438
                               55.816 15.269 10.645 1.00 42.25
    ATOM 1791 N PHE 439
10
                               54.957 15.170 9.479 1.00 42.81
    ATOM 1792 CA PHE 439
    ATOM 1793 CB PHE 439
                               53.593 15.790 9.771 1.00 42.18
                               52.594 15.597 8.656 1.00 42.48
    ATOM 1794 CG PHE 439
                                52.173 14.312 8.295 1.00 47.09
    ATOM 1795 CD1 PHE 439
                                52.086 16.696 7.961 1.00 39.76
    ATOM 1796 CD2 PHE 439
15
                                51.256 14.110 7.234 1.00 49.17
    ATOM 1797 CE1 PHE 439
    ATOM 1798 CE2 PHE 439
                                51.174 16.524 6.896 1.00 45.10
                               50.751 15.225 6.532 1.00 46.36
    ATOM 1799 CZ PHE 439
                               55.626 15.905 8.322 1.00 44.79
    ATOM 1800 C PHE 439
                               55.596 15.444 7.181 1.00 40.26
20
    ATOM 1801 O PHE 439
    ATOM 1802 N LEU 440
                               56.236 17.049 8.629 1.00 42.77
    ATOM 1803 CA LEU 440
                               56.927 17.839 7.621 1.00 42.96
                               57.421 19.156 8.216 1.00 37.19
    ATOM 1804 CB LEU 440
                                56.348 20.117 8.725 1.00 36.97
    ATOM 1805 CG LEU 440
                                57.020 21.338 9.321 1.00 33.65
    ATOM 1806 CD1 LEU 440
25
    ATOM 1807 CD2 LEU 440
                                55.411 20.519 7.572 1.00 35.42
                               58.106 17.063 7.053 1.00 45.47
    ATOM 1808 C LEU 440
                               58.421 17.191 5.876 1.00 52.48
    ATOM 1809 O LEU 440
                              58.760 16.266 7.890 1.00 49.15
    ATOM 1810 N HIS 441
                               59.893 15.473 7.435 1.00 54.76
    ATOM 1811 CA HIS 441
30
                               60.723 14.964 8.624 1.00 56.68
    ATOM 1812 CB HIS 441
                               61.515 16.026 9.323 1.00 62.73
    ATOM 1813 CG HIS 441
                               62.851 16.166 9.508 1.00 65.73
    ATOM 1814 CD2 HIS 441
                                60.929 17.098 9.966 1.00 66.01
     ATOM 1815 ND1 HIS 441
     ATOM 1816 CE1 HIS 441
                               61.871 17.845 10.518 1.00 65.55
35
                               63.044 17.306 10.258 1.00 60.09
     ATOM 1817 NE2 HIS 441
                              59.417 14.292 6.589 1.00 55.93
     ATOM 1818 C HIS 441
                              60.084 13.908 5.630 1.00 57.33
     ATOM 1819 O HIS 441
                               58.271 13.716 6.948 1.00 57.81
     ATOM 1820 N MET 442
                                57.712 12.585 6.203 1.00 59.11
     ATOM 1821 CA MET 442
40
                                56.562 11.924 6.978 1.00 55.93
     ATOM 1822 CB MET 442
                                56.961 11.246 8.276 1.00 58.52
     ATOM 1823 CG MET 442
                                55,564 10.420 9.105 1.00 60.99
     ATOM 1824 SD MET 442
                                54.430 11.779 9.350 1.00 52.61
     ATOM 1825 CE MET 442
                               57.178 13.065 4.854 1.00 60.31
     ATOM 1826 C MET 442
                               57.279 12.369 3.846 1.00 58.18
     ATOM 1827 O MET 442
                               56.608 14.266 4.863 1.00 61.45
     ATOM 1828 N LYS 443
                                56.038 14.871 3.669 1.00 64.90
     ATOM 1829 CA LYS 443
                                55.434 16.232 4.035 1.00 64.40
     ATOM 1830 CB LYS 443
                                54.589 16.872 2.945 1.00 69.12
     ATOM 1831 CG LYS 443
50
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	ATOM	1832 CD LYS 443	54.064 18.250 3.363 1.00 71.14
	ATOM	1833 CE LYS 443	
	ATOM	1834 NZ LYS 443	52.668 19.534 5.015 1.00 67.97
		1835 C LYS 443	57.112 15.030 2.585 1.00 67.29
_	ATOM		56.800 15.218 1.406 1.00 67.90
5	ATOM	1836 O LYS 443 1837 N VAL 444	58.373 14.941 2.996 1.00 66.57
	ATOM		
	ATOM	1838 CA VAL 444	59.501 15.064 2.078 1.00 64.76
	ATOM	1839 CB VAL 444	60.618 15.940 2.693 1.00 62.76
	ATOM	1840 CG1 VAL 444	61.767 16.092 1.712 1.00 64.00
10	ATOM	1841 CG2 VAL 444	60.062 17.301 3.072 1.00 59.27
	ATOM	1842 C VAL 444	60.091 13.693 1.744 1.00 68.61
	ATOM	1843 O VAL 444	60.145 13.294 0.577 1.00 70.60
	ATOM	1844 N GLU 445	60.520 12.972 2.775 1.00 70.71
	ATOM	1845 CA GLU 445	61.129 11.653 2.609 1.00 71.45
15	ATOM	1846 CB GLU 445	61.808 11.233 3.916 1.00 72.36
	ATOM	1847 C GLU 445	60.181 10.547 2.148 1.00 71.46
	ATOM	1848 O GLU 445	60.588 9.390 2.042 1.00 73.02
	ATOM	1849 N CYS 446	58.925 10.895 1.871 1.00 71.12
	ATOM	1850 CA CYS 446	57.945 9.901 1.419 1.00 70.83
20	ATOM	1851 CB CYS 446	57.031 9.485 2.581 1.00 71.05
	ATOM	1852 SG CYS 446	57.845 8.593 3.925 1.00 72.83
	ATOM	1853 C CYS 446	57.081 10.390 0.261 1.00 71.91
	ATOM	1854 O CYS 446	56.776 11.582 0.155 1.00 72.06
	ATOM	1855 N PRO 447	56.673 9.470 -0.635 1.00 73.12
25	ATOM	1856 CD PRO 447	56.967 8.026 -0.671 1.00 72.88
	ATOM	1857 CA PRO 447	55.837 9.825 -1.784 1.00 74.22
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	ATOM	1860 C PRO 447	54.479 10.343 -1.330 1.00 75.94
30	ATOM	1861 O PRO 447	53.754 9.652 -0.616 1.00 76.67
50	ATOM	1862 N THR 448	54.145 11.558 -1.755 1.00 76.91
	ATOM	1863 CA THR 448	52.879 12.197 -1.403 1.00 78.24
	ATOM	1864 CB THR 448	52.647 13.459 -2.261 1.00 81.33
	ATOM	1865 OG1 THR 448	52.552 13.087 -3.643 1.00 84.46
35	ATOM	1866 CG2 THR 448	53.802 14.444 -2.089 1.00 83.51
33	ATOM	1867 C THR 448	51.676 11.270 -1.580 1.00 77.42
	ATOM	1868 O THR 448	50.662 11.413 -0.894 1.00 77.65
		1869 N GLU 449	51.795 10.319 -2.502 1.00 76.29
	ATOM		50.720 9.375 -2.783 1.00 75.03
40	ATOM	1870 CA GLU 449	
40	ATOM	1871 CB GLU 449	
	ATOM	1872 C GLU 449	50.445 8.421 -1.622 1.00 73.49
	ATOM	1873 O GLU 449	49.310 7.973 -1.442 1.00 70.24
	ATOM	1874 N LEU 450	51.477 8.113 -0.840 1.00 70.80
	ATOM	1875 CA LEU 450	51.327 7.194 0.285 1.00 68.82
45	ATOM	1876 CB LEU 450	52.693 6.644 0.705 1.00 71.91
	ATOM	1877 CG LEU 450	53.428 5.795 -0.336 1.00 76.62
	ATOM	1878 CD1 LEU 450	54.799 5.414 0.195 1.00 77.95
	ATOM	1879 CD2 LEU 450	52.617 4.546 -0.662 1.00 76.46
	ATOM	1880 C LEU 450	50.636 7.818 1.492 1.00 66.22
50	ATOM	1881 O LEU 450	50.501 7.181 2.540 1.00 66.01

	ATOM	1882 N PHE 451	50.189 9.060 1.342 1.00 61.96
	ATOM	1883 CA PHE 451	49.513 9.750 2.428 1.00 58.44
	ATOM	1884 CB PHE 451	50.006 11.204 2.528 1.00 61.34
	ATOM	1885 CG PHE 451	51.466 11.343 2.923 1.00 63.02
5	ATOM	1886 CD1 PHE 451	52.488 10.888 2.077 1.00 62.92
•	ATOM	1887 CD2 PHE 451	51.812 11.932 4.146 1.00 63.07
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	ATOM	1889 CE2 PHE 451	53.167 12.085 4.531 1.00 64.66
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10	ATOM	1891 C PHE 451	48.005 9.756 2.219 1.00 56.41
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	ATOM	1893 N PRO 452	47.260 8.954 3.009 1.00 53.28
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15	ATOM	1896 CB PRO 452	45.388 7.976 4.000 1.00 49.19
,	ATOM	1897 CG PRO 452	46.558 7.010 4.039 1.00 45.89
	ATOM	1898 C PRO 452	45.183 10.305 2.974 1.00 49.62
	ATOM	1899 O PRO 452	45.727 11.176 3.644 1.00 52.35
	ATOM	1900 N PRO 453	44.034 10.530 2.313 1.00 51.50
20	ATOM	1901 CD PRO 453	43.257 9.585 1.494 1.00 49.66
	ATOM	1902 CA PRO 453	43.354 11.830 2.335 1.00 50.89
	ATOM	1903 CB PRO 453	42.101 11.559 1.506 1.00 51.49
	ATOM	1904 CG PRO 453	42.600 10.524 0.521 1.00 50.82
	ATOM	1905 C PRO 453	43.030 12.405 3.706 1.00 50.99
25	ATOM	1906 O PRO 453	43.264 13.588 3.953 1.00 54.17
	ATOM	1907 N LEU 454	42.479 11.576 4.592 1.00 51.21
	ATOM	1908 CA LEU 454	42.112 12.034 5.936 1.00 47.17
	ATOM	1909 CB LEU 454	41.305 10.951 6.660 1.00 44.44
	ATOM	1910 CG LEU 454	40.748 11.283 8.050 1.00 41.33
30	ATOM	1911 CD1 LEU 454	39.838 12.504 7.978 1.00 35.93
	ATOM	1912 CD2 LEU 454	39.986 10.072 8.587 1.00 34.79
	ATOM	1913 C LEU 454	43.363 12.380 6.733 1.00 42.25
	ATOM	1914 O LEU 454	43.387 13.357 7.475 1.00 40.82
	ATOM	1915 N PHE 455	44.399 11.567 6.565 1.00 39.29
35	ATOM	1916 CA PHE 455	45.674 11.774 7.240 1.00 41.81
	ATOM	1917 CB PHE 455	46.655 10.679 6.802 1.00 47.22
	ATOM	1918 CG PHE 455	48.045 10.800 7.407 1.00 56.97
	ATOM	1919 CD1 PHE 455	48.220 10.990 8.785 1.00 57.23
	ATOM	1920 CD2 PHE 455	49.180 10.645 6.597 1.00 59.40
40	ATOM	1921 CE1 PHE 455	49.522 11.030 9.362 1.00 56.58
	ATOM	1922 CE2 PHE 455	50.487 10.682 7.149 1.00 61.80
	ATOM	1923 CZ PHE 455	50.656 10.870 8.541 1.00 59.94
	ATOM	1924 C PHE 455	46.203 13.161 6.892 1.00 45.12
	ATOM	1925 O PHE 455	46.558 13.944 7.779 1.00 39.95
45	ATOM	1926 N LEU 456	46.236 13.471 5.592 1.00 43.92
	ATOM	1927 CA LEU 456	46.704 14.767 5.123 1.00 44.08
	ATOM	1928 CB LEU 456	46.748 14.795 3.593 1.00 50.20
	ATOM	1929 CG LEU 456	47.796 13.921 2.903 1.00 55.79
	ATOM	1930 CD1 LEU 456	47.527 13.869 1.408 1.00 54.70
50	ATOM	1931 CD2 LEU 456	49.187 14.473 3.193 1.00 53.01

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                               44.500 15.549 5.726 1.00 44.56
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    ATOM 1935 CA GLU 457
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                               42.138 15.854 6.133 1.00 50.16
                               43.759 17.039 7.579 1.00 43.60
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    ATOM 1938 O GLU 457
                               43.867 18.245 7.795 1.00 42.69
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    ATOM 1940 CA VAL 458
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    ATOM 1941 CB VAL 458
10
                                44.180 15.510 12.277 1.00 49.72
    ATOM 1942 CG1 VAL 458
    ATOM 1943 CG2 VAL 458
                                42.708 14.427 10.567 1.00 40.89
    ATOM 1944 C VAL 458
                               45,368 17.178 10.209 1.00 42.72
                               45.393 18.139 10.974 1.00 42.88
    ATOM 1945 O VAL 458
                              46.451 16.743 9.574 1.00 44.53
    ATOM 1946 N PHE 459
15
    ATOM 1947 CA PHE 459
                               47.741 17.366 9.823 1.00 48.18
                               48.784 16.269 10.064 1.00 43.60
    ATOM 1948 CB PHE 459
    ATOM 1949 CG PHE 459
                               48.374 15.276 11.133 1.00 40.79
                                47.835 14.032 10.783 1.00 41.01
    ATOM 1950 CD1 PHE 459
                                48.471 15.613 12.492 1.00 39.48
    ATOM 1951 CD2 PHE 459
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                               47.387 13.118 11.776 1.00 40.62
     ATOM 1952 CE1 PHE 459
                                48.032 14.715 13.506 1.00 36.87
    ATOM 1953 CE2 PHE 459
                               47.489 13.463 13.146 1.00 36.39
    ATOM 1954 CZ PHE 459
                              48.234 18.348 8.763 1.00 52.71
    ATOM 1955 C PHE 459
                               49.336 18.878 8.877 1.00 51.34
    ATOM 1956 O PHE 459
25
                               47.397 18.594 7.752 1.00 59.56
     ATOM 1957 N GLU 460
                               47.695 19.509 6.647 1.00 66.14
     ATOM 1958 CA GLU 460
                               47.818 20.944 7.158 1.00 67.76
     ATOM 1959 CB GLU 460
                                46.536 21.511 7.724 1.00 78.99
     ATOM 1960 CG GLU 460
     ATOM 1961 CD GLU 460
                                46.680 22.965 8.116 1.00 86.08
30
                                47.014 23.786 7.237 1.00 87.62
    ATOM 1962 OE1 GLU 460
                                46.460 23.289 9.301 1.00 91.63
     ATOM 1963 OE2 GLU 460
                               48,940 19.163 5.836 1.00 69.17
     ATOM 1964 C GLU 460
                               48.784 18.759 4.660 1.00 69.49
     ATOM 1965 O GLU 460
                                50.057 19.298 6.379 1.00 76.70
     ATOM 1966 OXT GLU 460
35
     ATOM 1967 C1 TRI 1
                             47.283 4.313 16.972 1.00 44.70
                             51.052 6.807 13.814 1.00 34.01
     ATOM 1968 C2 TRI
                             47.289 4.043 15.500 1.00 37.90
     ATOM 1969 C3 TRI
                        1
                             51.936 6.615 12.728 1.00 33.38
     ATOM 1970 C4 TRI 1
     ATOM 1971 C5 TRI
                             48.462 4.501 14.746 1.00 46.53
                          1
40
                             52.294 7.653 11.847 1.00 42.90
     ATOM 1972 C6 TRI
                         1
                             49.577 5.179 15.334 1.00 34.63
     ATOM 1973 C7 TRI
                             51.717 9.015 12.071 1.00 38.34
     ATOM 1974 C8 TRI
                          1
                             49.492 5.383 16.723 1.00 43.89
     ATOM 1975 C9 TRI
                         1
                             50.779 9.237 13.172 1.00 40.43
     ATOM 1976 C10 TRI
                         1
45
                             48.354 4.960 17.533 1.00 41.82
     ATOM 1977 C11 TRI
                          1
                              50.449 8.116 14.055 1.00 35.64
     ATOM 1978 C12 TRI
                          1
                            46.287 3.725 17.959 1.00 36.78
     ATOM 1979 C13 TRI
                         1
                              44.825 4.150 17.865 1.00 40.69
     ATOM 1980 C15 TRI 1
     ATOM 1981 I1 TRI 1 48.684 4.002 12.609 1.00 40.26
50
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	ATOM	1982 I2 TRI 1	53.597 7.174 10.336 1.00 46.70	
	ATOM	1983 I3 TRI 1	51.362 6.218 17.644 1.00 36.54	
	ATOM	1984 O3 TRI 1	44.546 5.255 17.329 1.00 54.78	
	ATOM	1985 O2 TRI 1	50.831 5.617 14.667 1.00 28.44	
5	ATOM	1986 O1 TRI 1	52.207 10.160 11.342 1.00 43.65	
	ATOM	1987 O4 TRI 1	44.021 3.333 18.352 1.00 42.95	
	ATOM	1 AS CAC 501	60.548 16.977 16.916 1.00 65.97	AS
	ATOM	2 AS CAC 502	27.863 16.627 16.796 1.00 89.34	AS
	ATOM	3 AS CAC 503	29.889 28.698 21.811 1.00100.00	AS
10	ATOM	4 AS CAC 504	33.547 24.203 8.880 1.00100.00	AS
	ATOM	5 O HOH 505	42.365 8.872 4.597 1.00 53.88	HOH
	ATOM	6 O HOH 506	33.545 30.973 24.585 1.00 40.33	HOH
	ATOM	7 O HOH 507	37.040 1.824 12.671 1.00 61.87	HOH
	ATOM	8 O HOH 508	44.105 4.635 6.023 1.00 40.68	HOH
15	ATOM	9 O HOH 509	52.686 13.817 -6.263 1.00 54.00	HOH
	ATOM	10 O HOH 510	50.186 12.691 -5.997 1.00 55.36	HOH
	ATOM	11 O HOH 511	49.278 18.540 14.006 1.00 34.79	HOH
	ATOM	12 O HOH 512	25.541 28.885 21.206 1.00 55.42	HOH
	ATOM	13 O HOH 513	27.346 31.063 27.398 1.00 58.30	НОН
20	ATOM	14 O HOH 514	40.790 19.192 39.234 1.00 50.35	НОН
20	ATOM	15 O HOH 515	37.467 0.637 37.293 1.00 37.46	НОН
	ATOM	16 O HOH 516	36.155 3.879 47.189 1.00 61.37	НОН
	ATOM	17 O HOH 517	35.410 5.865 50.995 1.00 63.46	НОН
	ATOM	18 O HOH 518	33.622 5.440 47.570 1.00 53.87	НОН
25	ATOM	19 O HOH 519	64.787 6.888 11.882 1.00 51.15	НОН
23	ATOM	20 O HOH 520	61.109 -8.688 27.722 1.00 61.70	НОН
	ATOM	21 O HOH 521	49.869 -5.472 30.343 1.00 40.50	НОН
	ATOM	22 O HOH 522	43.786 -0.987 26.878 1.00 52.16	НОН
	ATOM	23 O HOH 523	41.604 2.361 26.985 1.00 47.90	НОН
20		24 O HOH 524	54.405 6.361 39.795 1.00 56.56	НОН
30	ATOM		46.088 0.770 33.095 1.00 74.24	НОН
	ATOM		50.481 16.245 15.314 1.00 28.99	НОН
	ATOM	26 O HOH 526		НОН
	ATOM	27 O HOH 527		НОН
2.5	ATOM	28 O HOH 528		НОН
35	ATOM	29 O HOH 529		HOH
	ATOM	30 O HOH 530	56.701 9.852 30.561 1.00 51.24	
	ATOM	31 O HOH 531	26.487 13.273 30.591 1.00 43.94	HOH
	ATOM	32 O HOH 532	27.019 25.052 28.330 1.00 54.97	HOH
	ATOM	33 O HOH 533	50.689 1.918 29.551 1.00 30.63	НОН
40	ATOM	34 O HOH 534	47.867 0.200 31.330 1.00 43.14	НОН
	ATOM	35 O HOH 535	61.434 -0.721 23.218 1.00 49.83	НОН
	ATOM	36 O HOH 536	41.969 20.017 20.894 1.00 27.00	НОН
	ATOM	37 O HOH 537		НОН
	ATOM	38 O HOH 538		НОН
45	ATOM	39 O HOH 539		HOH
	ATOM	40 O HOH 540		НОН
	ATOM	41 O HOH 541	43.310 1.560 41.912 1.00 43.56	HOH
	END			

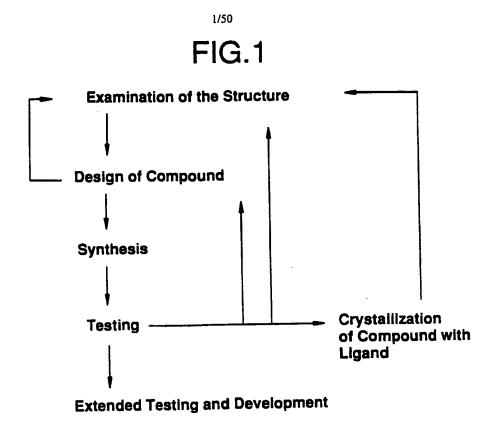


FIG.2

DOMAINS : NH2-TERMINAL	DNA BINDING	LIGAND BINDING
HOMOLOGY: Hypervariable	> 40%	About 20%
FUNCTION: Transactivation	DNA Binding Dimerization	LIGAND Binding Dimerization Transactivation Nuclear translocation Hsp binding

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2/50 VSCVSGAIPN IPISLDGLLF TSDTLPEVSA DENNYMEIVN PAAGPFPGSQ RWGQVSQAVE RSSLGPTERT PEVGSPLLCR SLPEGLOMER APHVAGGPPS HTELKAKGPR ... HETKGYH hPR her hGR HAR HAR hvdr hPPARgamma **hRARgamma** hRXRalpha hRXRbeta hPPARalpha **hPPARbeta** hTRbeta hRARalpha rTRalpha hTRalpha

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			~	FIG 3R			
		•	•	•	•		har
	YHDSVRDADY	SATVAESHGL	IKTELESKEL	NNRPGILTSD	GSSKEK QELLPCLQQD	NSTOGSSKEK	NMR
	LDSVLDTLLA		EATRGAGGSS	SDVEGAYSRA	DEKTODOOSL	PRPCQGQDPS	hPR
	VALLENG		SLTPGREENP	MDSKE	•	• • • • • • • • • • • • • • • • • • • •	hGR
			•	•	•	•	her
	•	• • • • • • • • • • • • • • • • • • • •	•	•	•	•	hvdr
	•	•	•	•	•	•	hPPARgamma
	•	• • • • • • • • • •	•	•	•	•	hPPARbeta
	•	•	•	•	•	•	hPPARalpha
0	•	•	•	•	• • • • • • • • • • • • • • • • • • • •	•	hRXRbeta
3/5	•	• • • • • • • • • • • • • • • • • • • •	•	•	•	•	hRXRalpha
	•	• • • • • • • • • • • • • • • • • • • •	•	•	•	•	hRARgamma
	•	•	•	•	•	•	hRARalpha
	• • • • • • • • • • • • • • • • • • • •	•	•	•	•	•	hTRbeta
	•	• • • • • • • • • •	•	•	•	•	hTRalpha
	•	•	•	•	•	•	rTRalpha
	120					61	

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4/50 KVGDSSGTAA SDSGSSVNGG DFPKGSVSNA LSPLMSRSGC . DSKQRRLLV PPAAPATORV GHRPSTLSCV EQLVKFYKGN CLFGPELPED **MSPAKIYQNV PPACEVTSSW** PSLAVASQS. GATVKVSASS SYEQUNQQCS PSGPGQSQPS 121 hVDR hGR hPR her P. R. R. hTRalpha hRARalpha hRXRalpha hRXRbeta hPPARalpha hPPARbeta hPPARgamma rTRalpha hTRbeta hRARgamma

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						5	/50					
240	•	•	•	•	•	•	• • • • • • • • • • • • • • • • • • • •	• • • • • • • • • • • • • • • • • • • •	• • • • • • • • • • • • • • • • • • • •		•	ESIANLNRS. ESAGPLLKGK PVHSPITQGT
	•	•	•	•	• • • • • • • • • • • • • • • • • • • •	• • • • • • • • • • • • • • • • • • • •	•	•	•	•	•	SGETDLKLLE VEEDSSESE SSTTASFGSF
	•	•	•	•	•	•	•	•	•	•	•	FPQQCQISLS KPSPQAAAVE VCSPAGINSV
	•	•	•	•	•	•	•	•	•	•	•	ETKVMGNDLG ESPHWSGAPV VCSPLNHTSS
	•	•	•	•	•	•	•	•	•	•	•	LSMGLYHGET PARQLLLPAS PIHCHEKSPS
181	•	•	•	•	•	•	•	•	•	•	•	QQPDLSKAVS AHKVLPRGLS VHRAIVKS
-	rTRalpha	hTRalpha	hTRbeta	hRARalpha	hRARgamma	hRXRalpha	hRXRbeta	PPARalpha	hPPARbeta	PPARgamma	hVDR	her hgr hpr hmr

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6/50 PVSSPNNVIL GNVKLYTT. SPPSHCSVKS ALVEQDAPHA HLKGQTGTNG THSDVSSEQQ EDSRFSAPRV RGSRSHSPAH ASNVGSPLSS PLSSHKSSIS AAPTEKEFPK AAGGVALVPK PKSSASTAVS GGAAACPPGA ... TSVPEN PRALGGAAAG PLTCSPNAEN 241 hvdr her hGR hPR HAR HAR hPPARgamma hRARg amma hRXRalpha hRXRbeta hPPARalpha hPPARbeta rTRalpha hTRalpha hRARalpha

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7/50 TASGTSAGSS NESPWRSDLL CSPVNNAFSY SGSPGK... GGACAA.... SPAASTVGSI NNSRCSVSSP SNTNNRSTLS FDILQDLEFS RQLLEDESYDbosr LNHALLAART MDFIHVPILP RSSVSSPANI 301 hPR hHR hAR hGR hvdr her hPPARgamma hRXRbeta hPPARalpha hPPARbeta rTRalpha hTRalpha hTRbeta hRARa 1 pha hRARgamma hRXRalpha

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			3G	FIG 3G			
	•	•	•	•	•	•	har
	GAFSSSCEGG	IVQYIKPEPU	ISNGVIGQLN	FPKTEEVESA	DVVPSPD TQEKGAQEVP	TLRDVVPSPD	har.
	SARSFRSILV		YSDFQPPALK		P. DCAYPPD	SSTPVAVGDF	hPR
			ILPUTKPKIK	GNSNEDCKPL	GEDDSFLLE	IDENCLLSPL	hgR
	EVILO THENS		• 1		•	•	her
		•	•	•	• • • • • • • • • • • • • • • • • • • •		hvdr
	•	•	•	•	•	•	PPARgamma
	•	•	•	•	•	•	hPPARbeta
	•	•	•	•	•	•	PPARalpha
0,50	HAEUSVURNU	AAKFEFUR HAEGSVORNO	MSH · · · · ·	•	•	•	hRXRbeta
				• • • • • • • • • • • • • • • • • • • •	•	•	hRXRalpha
	•		•		•	•	hRARgamma
	•	•	•	•	•	•	hRARalpha
	•	•	•	•	•	•	hTRbeta
	•	•	•	•	•	•	hTRalpha
	•	•		• • • • • • • • • • • • • • • • • • • •	•	•	rTRalpha
	420					361	

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9/50 480 SRSPDSSSPN YPEGAAYEFN **HSAISVHGVS** PASASVSSAS KDYYSLSGIL TIRVLEVEVD VAPYGYTRP FSTQVNSSGA NY.... HSCSGISFKG NPIVNPFPFH DGSYFSFMDD LDSSKPAVYNA.A RDGRH..GRD AQVIVMSGQE MIKHFLPLD SCTLKFPAQD PLERPLGEVY PCACARGWIG ANIIG EAAVT....GG GGGEA..... TVYCQASFPG PR.ATPSRPG GGGGRRRITN EPLNRPQLKI PLTVNEQLLG AKECIVGSAT ALAGSRSGGG FPLGPPPPLP SVPIKQESTK PGVIKQEKLG DTEDLPANNA LLHQIQGNEL AGANPAAFPD TLHTKASGMA EKEDFIELCT NSKINSDSSF 421 hVDR her hGR hPR HAR **HAR** hPPARgamma hTRalpha hTRbeta hRARa l pha hRARgamma hRXRalpha hRXRbeta hPPARalpha hPPARbeta rTRalpha

FIG.3H

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	481					540
rTRalpha	•	•	•	•	MEQKPSK VECGSDPEEN	VECGSDPEEN
hTRalpha		•	•	•	HEQKPSK VECGSDPEEN	VECGSDPEEN
hTRbeta		•	MTPNSHTE	NGLTAWDKPK HCPDREHDWK LVGHSEACLH	HCPDREHDWK	LVGHSEACLH
hRARalpha	•	•		•	•	•
hRARgamma	•	• • • • • • • •	•	H ATNKERLFAA	ATNKERLFAA	GALGPGSGYP
hRXRalpha	.LTSPTGR	GSMAAPSLHP SLGPGIGSPG	SLGPGIGSPG	.QLHSPISTL SSPINGMGPP	SSPINGHGPP	FSVISSPHGP
hRXRheta	PLPOGVPP.	PSPPGPPLPP STAPTLGGSG	STAPTLGGSG	APPPP	PHPPPLGSP FPVISSSHGS	FPVISSSHGS
hppagalpha	. MVDTESPL		LESPLSEEFL	QEHGNIQEIS QSIGEDSSGS FGFTEYQYLG	QSIGEDSSGS	FGFTEYQYLG
hppanheta		MEQPO	EEAP	.EVREEEEKE	EVREEEEKE EVAEAEGAPE LNGGPQHALP	LNGGPQHALP
hppaRcamma		MVD	TEMPFWPTNF	GISSVD	GISSVD LSMADDHSHS	FDIKPFTTVD
ACDA	TALSSAGAAE	TALSSAGAAE SGGDEEGSGQ SLEATEEAQL DGPVTTSSTT AVTVEVSAPV	SLEATEEAQL	DGPVTTSSTT	AUTVEVSAPV	VQTVVSKAAI
her R	AAAAANAOVX	GOTGLPYGPG SEAAAFGSNG LGGFPPLNSV SPSPLMLLHP	SEAAAFGSNG	LGGFPPLNSV	SPSPLMLHP	PPQLSPFLQP
hGR	TSGGOMYHYD		DQ	.KPIFNVIPP IPVGSEN	I PVGSEN	•
hPR	SSGSTLECIL	YKAEGAPPQQ	GPFAPPPCKA	PGASGCLLPR DGLPSTS	DGLPSTS	•
hhr		PVPGFDGN CEGSGFPVGI KQEPDDGSYY	KQEPDDGSYY	PEASIPSSAI VGVNSGGQSF	VGVNSGGQSF	HYRIGAQGTI
hAR	•	PQGLAGQE SDFTAPDVWY PGGHVSR VPYPSPT	SDFTAPDVWY	PGGHVSR	VPYPSPT	•

FIG.3

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11/50 VSSSTLRSVS DKGSHAHESA .SSPPSSSST DSEASQSPQY YPWPGSVDE AQLYNRPHEE AGSVGCQGGL GLHCPPPGG DQLQHGC.DG **EEIVPSPPSP EEHVPSSPSP** VLKVPAHPSGSGYIsgxI TEEKKCKGYI GOPLLIPLSM FQHLSSFPPV NTLVESWKSH GDLSSRRSDG YPVLEYIPEN GGRERLASTN AVLKEGLPQV YPPYLNYLRP PYGD HRLETARDHV LP..IDYYFP .SSPS..SVT .sspp..sll PASPPYYSEK LSVETQSTSS DVKPPVLGVR QSVSSAQTFQ AAIETQSSSS DIKPPLGLNG YRPNSDNRRQ . PHNPVSSSE **QEYQSAIKVE** GYSSPSMRPD SNHVASGAGE QPDLPKEMAS LPGGGSGPPE TGHLAQQSSL • • • • • • • • • FHLOHDDVND NGLPQLGYQA LTQDGLASLM AGPP....AF NFPGRTVFSN SSPQINSTVS LIQTTWISSI HLSPSFRGLG VADYKYDLKL PN. LKSSHLKTSH GSPQLSS... • • • • • • • • • APALYPALGL NEPSGYTVRE DDNLTSLGTL **PITVQACPQV** ALR.GSPPFE DIPFTRADPM LKN. EQSSPH .TTPTLGFST WMDSYSG... . APPGFSGPV TDTLSPA... ...LSRS... SARSPOGKRK RKN. GQCP.. RKN.GQCS.. SLSRSARDQS . CVKSEMGP . ASAAAAGA SVSPAQQTSV HCQQVPYYLE . WNRCQGSG GAGFPFAFPG FSSISAPHYE RKSHSERRST HSMSVP.... PGLPPP.... SCPGSDGSVI SSSYTD... SARSPOGKRK 541 her hGR hPR 五品 hvdr HAR hPPARgamma hRXRalpha hPPARbeta hTRalpha hTRbeta **hRARgamma** hRXRbeta hPPARalpha rTRalpha hRARa 1 pha

FIG. 3.

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999 QAVLQPQMSA EG. NK... DK.. KGFFRRIIQK NLHPTYSCKY DS. NH..VYTCHR DL..TYSCRD KLIYD...RC KLVYD...KC KLEYE...KC SVQTQLQAPA NLHPTYSCKY NLHPSYSCKY NH.. VYTCHR DL..TYTCRD HN. DYHCPA QHNYLCAGRN OHNYLCAGRN QHNYLCAGRN KOKYLCASRN KGFFRRTIOK KGFFRRSIQK KGFFRRSIQK KVFFKRAAEG KGFFRRTIQK KGFFRATIRL KGFFRRTIRM AGLQAATVLN KAFFKRSIQG KVFFKRAVEG KVFFKRAMEG KVFFKRAVEG KGFFKRTIRK KGFFRRTIRL KGFFKRTVRK WCGDKATGY HYRCITCEGC LICGDKASGC HYGALTCGSC HYRCITCEGC FVCNDKSSGY HYGVSSCEGC HYGVYSCEGC PAGGLLKLPF HYGVLTCGSC HYGWTCGSC HYRCITCEGC HYGVSACEGC AICGDRSSGK HYGVYSCEGC HYGVHACEGC HYGVHACEGC HYGVHACEGC HYGVWSCEGC HYGVLTCGSC LVCSDEASGC LICGDEASGC LVCGDEASGC AICGDRSSGK VVCGDKATGY RVCGDKASGF ATLPGLAAAS AVCNDYASGY WCGDKATGY FVCQDKSSGY RICGDKASGY RVCGDKASGF PSYLDKDEQC KET...RYC ATTGPPPKLC **IGSSRPSKIC** PQKIC NMASFTKHIC SPSGALNIEC PSNSLMAIEC SFESLPOKIC PSYLDKDEQC PSYLDKDELC PPLPRIYKPC PPPRVYKPC PGAG.. KRLC AVLTLPTATV ASCGSLNMEC 601 hvdr her hGR hPR **hAR** 표표 hRARg amma hRXRalpha hRXRbeta hPPARbeta hPPARgamma hTRbeta hRARalpha hPPARalpha rTRalpha hTRalpha

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FIG.3K

720

RRK. . EEHIR

RKL I EQNRER

VLDDSKRVAK

RRR. . EELOK KKK. EVPKP KKK. EVKEE EVE..STSSA DGE..CAGGA LKA. . EILTC LVA..GLTAN LLA. . EI. SS

RRK. EEHIR

VLDDSKRVAK RKLIEGNRER

CIAVGMAMDL

CCVIDKITR NQCQLCRFKK

rTRalpha hTRalpha hTRbeta

661

CIAVGHAMDL CIYVGMATDL CFEVGHSKES CFEVGMSKEA

NOCOLCRFKK

.CCVIDKITR

NOCOECRFKK NRCQYCRLQK CLAHGHKREA

NRCQYCRLQK NRCQYCRYQK

NCIINKVTR

hRARgamma hRXRalpha hRXRbeta hPPARalpha hPPARbeta

hRARalpha

NCIINKVTR

KCVIDKVTR

CLATGHKREA

CLSVGMSHNA

NKCQYCRFHK NKCQYCRFQK

NRCQYCRYQK

DCTVDKRQR SCKIQKKNR

DCLIDKROR

CLALGMSHNA

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LQE..EGEAS

GIH. . EEQPQ

.....RNK RKLKKLGNLKRNK KDRNEN ...KDK.DG . RHPEAEKRK . RHPOAEKEK LKHKRQRDDG RKTKK..KIK RKFKKFNKVR RKSKKLGKLK RKL I EENREK . RHPRSEKAK AIISAASLGA VLDDSKRLAK LQTAGLSINP CYEVGHHKGG IRKDRRGGRH VRND.... IRFG.... IRFG.... VQEERQRG.. IRFG.... VRUD.... VQEERQRG..

CLAVGHSHNA

ASEPSVSVAT

AATTASIVQK

LOAMOOTOTT

hvdr

.QCTIDKNRR

her hgr

.CIIDKIRR .CIVDKIRR

NKCQYCRFQK

SCKIQKKNR

NCRIHKKSR.

hPPARgamma

KSCQACRLRK KNCPACRYRK KNCPACRLRK KNCPACRLQK KNCPSCRLRK

CLQAGMNLEA

CLQAGMNLGA

CCQAGHVLGG

CYEAGHTLGA

.. CTIDKFRR

.CIIDKIRR

FAR AAR

hPR

EGR. GEVGS QPQFISSLTT

GIQ..QAIT.

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FIG.3

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14/50 780 INDMETICHA IHDIETLWOA IYDHNSLAMGLPA LL.... GKASNNPPFV GKTTDKSPFV SRALTPSPVH CKASHTAPFV • • • • • • • • • EPPILYSE.. SHWKORRKFL PDDIGOSPIV PDDICOSPIV PEDIGQAPIV TNNSSEQRV. TNSSADHRV.SP...SP... GAAAASA... DOMVSALLDA SHWKORRKFL SHWKOKPKFL CQL...GKYT CQL...GKYT TKAKARAILT PLLVNPASLA GLNPS.... GGSGS.... NKVKARVILS TKKKARSILT PPLIN.... TALVPQLSTI PTLVS.... PIFLN.... IAPAKEPSVN ETYVE..ANH DQGVEGPGGT EAYLKNFN. H NAYLKNFN. H NAQCOVICTE IVPATLPQLT VSHIEGYECQ EAHRSTNAQG DSYIKSFP.L KNSLALSLTA FSPCQDIQLI EAHRSTNAQG EAHVATNAQG KAHQETFPAL KAHQETFPSL TEETTOKLT EEWDLIHVAT EVGELIEKVR **QLEELITKVS** EAELAVEQKS DLKAFSKHIY TPI TSAMSN VAGLTSQLIT PSPLMIKRSK ETSENPGNKT ESQALSQRFT POSPEEGITY EEWDLIHIAT EEWELIKTUT EAELAVEPKT DLKSLAKRIY DLRALAKHLY minimal start site 725 SLOCKPEPTP SLOGRPEPTP DIDQLNPESA AGDHRAANLW ALPOPLGVPN 2000 PPPPPP SIGHKPEPTD ECSESYTLTP GSPUSYELSP NEDMPVERIL PEEMPVDRIL EHDIEDSETA EGSQYNPQVA ..GVSQ STT\$P.... 721 hVDR her hGR hPR **h**MR HAR hPPARgamma rTRalpha **hRARgamma** hRXRalpha hRXRbeta hPPARalpha hPPARbeta hTRalpha hTRbeta hRARalpha

FIG.3M

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LTLHDQVHLL LHLDDQMTLL LPLEDQITLI LHVDDQHAVI LPLDDQVILL LPENDOVTEL LDLNDQVTLL TTTOCPVCKV LHIDDQITLI LTIADQITLL LSIADQITLL LPLDDOVILL FAKKLPHFSE LPCEDQIILL LPCEDQIILL LPCEDQIILL LDLNDQVTLL GHDNNQPDSF AALLSSLNEL GERQLVHVVK WAKALPGFRN FAKKLPHFCE FAKRLPGFTG YAKNIPGFIN WAKVLPGFKN FAKKLPHFSE FAKQLPGFTT WAKRIPHFSS FAKSIPSFSS KATVPLTLTK WAKRVPGFVD WAKAIPGFRN WSKSLPGFRN HAKRIPHFSE FAKAIPAFAN ACKOMIQVVK ITPAITRVVD ITPAITRWD ITPAITRVVD AIPSTASVLP **GGRQVIAAVK** GERQLLSVVK STKCIIKTVE ADKQLFTLVE ADKQLFTLVE SVETVTELTE TVETVRELTE SVEAVQEITE ADRELVHMIN ATKCIIKIVE ENLLSTLNRL SSLLTSLNQLQLD LGLWDKFSEL IATIGNGPTA ASHMGLLTNL WRIHTTLNML . SMPDGDKVD LEAFSEFTKI LEAFSEFTKI .NAPEGGKVD LEAFSHFTKI IDLWDKFSEL VRIFHCCQCT VHVFYRCQCT IRIFOGCOFR A A A..... GYDSSKPDTA YDPTRPFSE . SMPDGDKVD OTS.... .NDPVTNICQ PLQEQSKEVA GYDSSVPDST CHDNTKPDTS NGION. KEVE NGLPPYKEIS .NDPVTNICQ **OLLLNSQGQI** ENIEPEIVYA EAIEPGUVCA **MSIEPDVIYA** EVIEPEVLYA EKTLVAKLVA EKGLVWKQLV EDKIKFKHIT **2GLQVQTVAP** • • • • • • • • • • • • • • • • 781 her hGR hPR **hAR** hvdr 돐 hTRalpha hTRbeta hRXRalpha hPPARalpha hPPARbeta **hPPARgamma** rTRalpha hRXRbeta hRARalpha **hRARgamma**

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FIG. 3N

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16/50 LCLTHWQIPQ **QCVRHRHLSQ** FDRVLTELVS FUMLLAT. SS **OCKHMLYVSS** LCQGMHQISL ..N..GGLGV VSDAIFELGK VSDAIFELGK VSDAIFDLGH LTDLVFAFAN LTDLVFAFAG FDRVLTELVS IHEPKFDFAH FHEPKFEFAV I IEPKFEFAV NLEEIREFAK ..N..AGFGP .. SLRKPFSD ... ESSFYS ...QSAMYE ..N..AGFGPLPCMYDKSRMYS ..N..GGLGV ..N..GGLGV .. S. AGVGAI .. S. AGVGAI .. SLRKPFCD .. SLRKPFGD PSAVKDEEAI .. CVEGHVEI HPTVGQLVNK F. HTREFLK. LVFNEEKHH. AMGWRSFINV NSRMLYFAPD LVFNEYRHH. LHVHRNSAH. F. ITREFLK. LLLDRNOGK. LIINEORHT. LILNEORHK. MIVKRKOLK. HAVIRGOLK. LTLNRTQMH. LTLNRTQMH. LHVHRNSAH. F. VTREFLR. HAVKREQLK. SANLLCFAPD SGOMLYFAPD NSQFLYFAPD ESDILILSGE EQDIMIFSDG EQUIMIFSDG VKDGILLATG VRDGILLATG DCMLVAYGNG DCLLVANGSG DGVLISEGQG TAAGVIACGE HPGKLLFAPN ESDTLTLSGE ESETLTLNGE ALSWRSYKHT RICTRY..TP SFSHRS..ID HLSSVH..NK MLASIV. .NK HLASLH..NK PSVVKPVTSL GLVWRS..HE GLGWRSYKHV SFSHRS..IA ALGWRSYRQS RAAVRY..DP RAAVRY..DP RICTRY..TP RAAVRY..DP **QY SWHGLHVF** QYSWMCLSSF QYSWHSLHVF APSKVIIAPQ OYSWMFLMAF RAGWNELLIA KYGVYEAIFA KYGVHEAIFA KYGVHEIIYT KGCCMEIMSL KAACLDILIL RAGWNELLIA ECAWLEILMI KGCCMEIMSL KGCCMEIMSL KAACLDILML 841 hvdr her hGR hPR PHR H HAR hPPARgamma hPPARalpha hPPARbeta rTRalpha hTRalpha hTRbeta hRARalpha hRARgamma hRXRalpha hRXRbeta

FIG. 3C

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							17/	50								
960	LAFEHYV	LAFEHYV	LAFEHYI	EALKVYV	EALRLYA	ASLEAYC	ASLETYC	HVLRLHL	RALEFHL	QALELQL	PVLERWLAEA	DTLIHLMAKA	KELGKAIVKR	RELIKAIGLR	KELRKHVTKC	KELDRIIACK
	KIEKSQEAYL	KIEKSQEAYL LAFEHYV	RPGLACVE RIEKYQDSFL LAFEHYI	RQDLEQPD RVDMLQEPLL EALKVYV	RMDLEEPE KVDKLQEPLL EALRLYA	KHRDMQHDKT ELGCLRAIVL FNPDSKGLSNPA EVEALREKVY ASLEAYC	KHRDMRMDKT ELGCLRAIIL FNPDAKGLSNPS EVEVLREKVY ASLETYC	RPGLLNVG HIEKMQEGIV HV LRLHL	KFNALELDDS DLALFIAAII LCGDRPGLMNVP RVEAIQDTIL RALEFHL	KFNALELDDS DLAIFIAVII LSGD RPGLLNVK PIEDIQDNLL QALELQL	NFKIRRLSLG LIQIQVGQAL TATEGPAYSQ SAICRFEKLD ITPKSAQKLK PVLERWLAEA	RFRHMNLOGE EFVCLKSIIL LNSGVYTFLS STLKSLEEKD HIHRVLDKIT DTLIHLMAKA	ELHRLOVSYE EYLCHKILL LSS VPKDGLKSQE LFDEIRMIYI KELGKAIVKR	IPLEGLRSQT QFEEMRSSYI RELIKAIGLR	OFVRLOLIFE EYTIHKVILL LST IPKDGLKSQA AFEEHRINYI KELRKHVIKC	IPVDGLKNQK FFDELRMNYI KELDRIIACK
	RSGLLCVD	RSGLLCVD	RPGLACVE	RQDLEQPD		KGLSNPA	KGLSNPS	RPGLLNVG	RPGLMNVP	RPGLLNVK	SAICRFEKLD	STLKSLEEKD	VPKDGLKSQE	IPLEGLRSQT	IPKDGLKSQA	IPVDGLKNQK
	MSTD	HSTD	MSSD	icgp	ICGD	FNPDS	FNPDA	cccb	LCGD	LSGD	TATEGPAYSQ	LNSGVYTFLS	LSS	LNT	LST	FSI
	EVALLQAVLL	SLSAFNLDDT EVALLQAVLL HSTD	SLSSFNLDDT EVALLQAVLL MSSD	ETGILSAICL ICGD	OLLPLEMDDT ETGLISAICL	ELGCLRAIVL	ELGCLRAIIL	DISLEVAAII CCGD	DLALFIAAII	DLAIFIAVII	LTQTQVGQAL	EFVCLKSIIL	EXLCMKTLLL	EFVKLOVSOE EFLCHKVILL LNT	EYTIHKVLLL	EFGWLQITPQ EFLCHKALLL FSI
901	SLSAFNLDDT EVALLQAVLL HSTDRSGLLCVD KIEKSQEAYL LAFEHYV	SLSAFNLDDT	SLSSFNLDDT	QLLPLEMDDA	QLLPLEMDDT	KHRDHQHDKT	KMRDMRMDKT	KFNALELDDS	KFNALELDDS	KFNALELDDS	NFKIRRLSLG	RFRHMINLOGE	ELHRLOVSYE	EFVKLOVSOE	OFVRLOLIFE	EFGWLQITPQ
	rTRalpha	hTRalpha	hTRbeta	hRARalpha	hRARgamma	hRXRalpha	hRXRbeta	hPPARalpha	hPPARbeta	hPPARgamma	hvdr	her	hGR	hPR	hwr	har

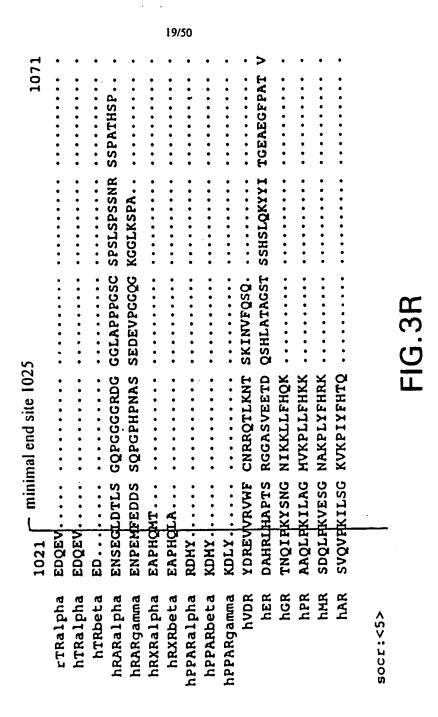
FIG.3F

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18/50 EITEIAKELN EFPEHMSEVI EFPAMLVEII DFPEMMAEII EFPEMLAEII SLHPLLQEIY PLYDLLLEML LFPPLFLEVF LFPPLFLEVF LLPPLFLEVF H. PPLIQEML H. PPLIREML PIDTFLMEML PIDTFLHEM ALHPLLQEIY SLHPLLQEIY RESHA..LKV IQSRA..LSV IKSHM..VSV CHASRFL..H MKVEC..PTE HKVEC..PTE LKHEI..PGS LKMEI..PGP FKL. I.. GDT IKKTE..SDA IKKTE..TET IKKTE..TDM FEKNSLPTGQ HKC.K..NVV LD.KT..HSI HKVEC..PTE FKL. I.. GDT CHASRFL..H KCLEHLF..F EHAQLVQ..I EHAQHMQ..R EHVQLLH..V PQAIEVLNTY NLLNYCFQTF **QLHLYCLNTF** DLLEFCFYTF LLDSVQPIAR ELHQFTFDLL KGAERAI..T KCLEHLF..F KGMEHLY..S CHASRFL..H KGAERVI..T ILSHIRHMSN LLDSMHDLVS KITDLRSISA RLPALRSIGL KMADLRQLVT KHTDLRQIVT KKRKRRTSFT LLDSMHEVVE LLDNLHDLVK KVTDLRHIGA KITDLRGIST RLPALRSIGL KMADLRQLVT KVTDLRHIGA KVTDLRMIGA FYQLT...K FAKVL...Q LHEFVGGEPS LAQLL...L FYQLT....K FYQLT...K FYQLT....K FPKLL...Q FPKML...H FPRML...H FPKLL...Q WPKLL...H FAKLL...L WPKLL...H WPKLL...H FAKLL...L PNNSGQSWQR KOKYPEQQGR QANHPDAQYL GLTLQQQHQR EGNSSQNWQR QKGVVSSSQR RKNPTSCSRR RRRRPSQPYH QSNHPDDIFL ELWNQKGQQN KHKYPEQPGR KLNHPESSQL NHRKHNIPHF NHRKHNIPHF NYRKHHVTHF RKRRPSRPHM hvdr her hcR hPR **h**HR HAR hPPARbeta hPPARgamma hTRalpha hTRbeta hRARalpha hRARgamma hRXRalpha hRXRbeta hPPARa 1 pha rTRalpha

FIG.30

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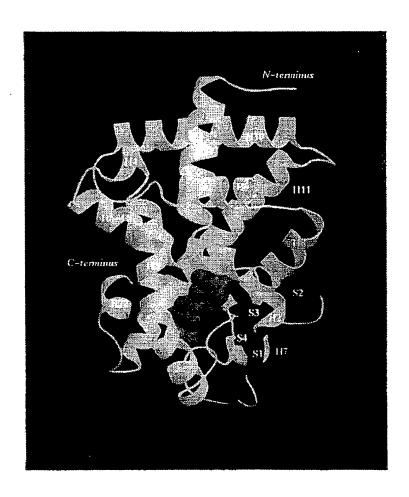
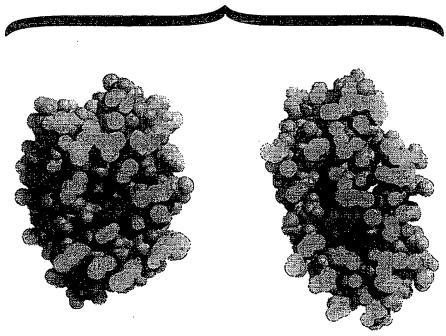


FIG.4

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FIG. 5



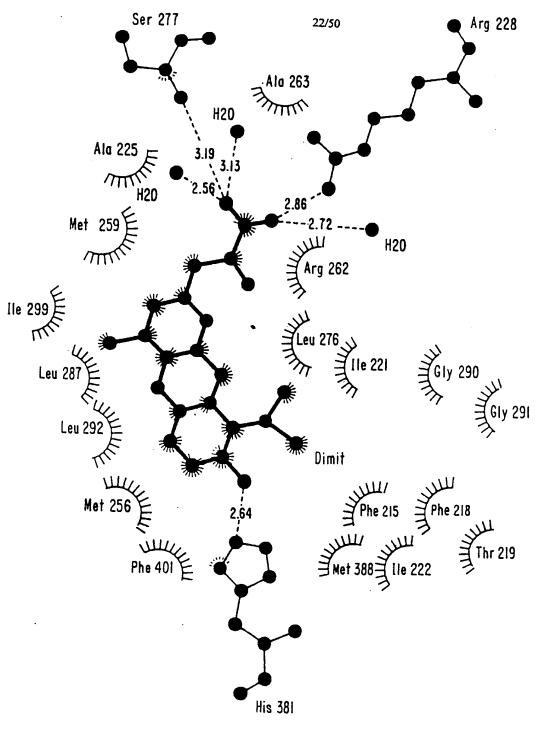


FIG.6

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FIG.7

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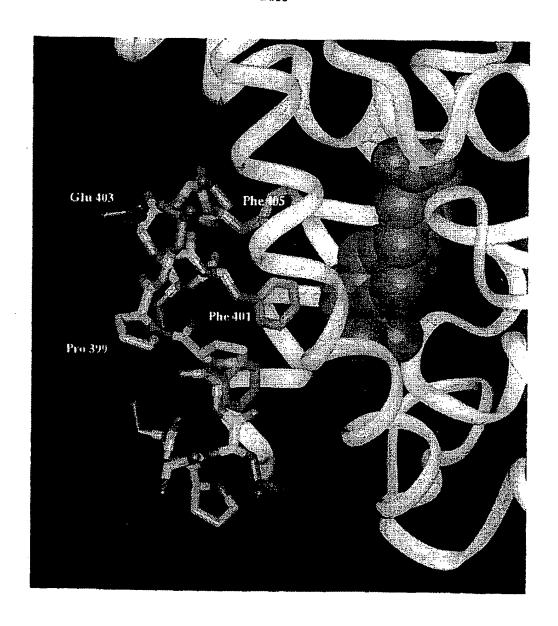


FIG.8

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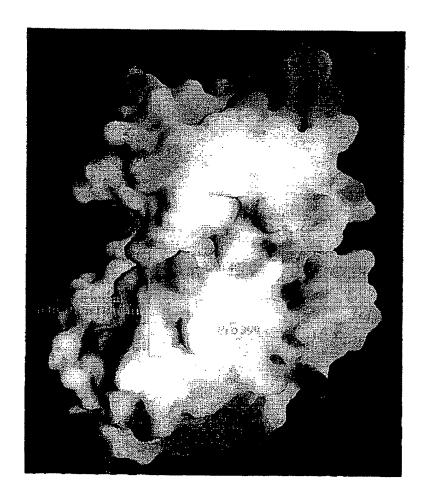


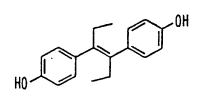
FIG.9

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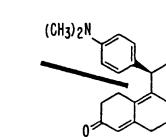
AGONISTS

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Retinoic Acid



Diethylstilbestrol



Progesterone

RU 486

FIG.10

shows position of extension group

Compound	RUUX
TSI	Ph2CHCO2NHS
TS2	C ₁₆ H ₃₃ CO ₂ NHS
TS3	FMOC-CI
TS4	tB 0C ₂ 0
TS5	tB0020

FIG.11

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SUBSTITUTE SHEET (RULE 26)

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FIG. 13

FIG. 14A

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FIG. 14B

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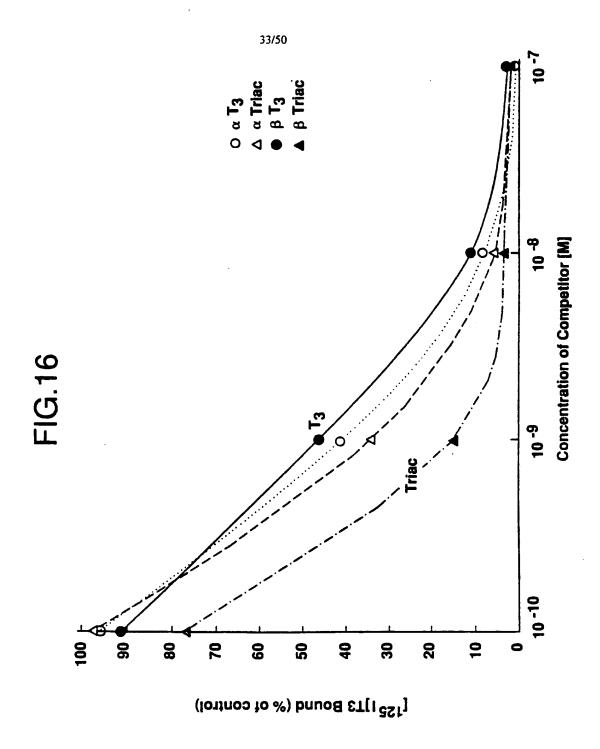
$$HO \longrightarrow 0 \longrightarrow NH_2$$

$$CO_2H$$

$$TS-9$$

FIG.15

SUBSTITUTE SHEET (RULE 26)



SUBSTITUTE SHEET (RULE 26)



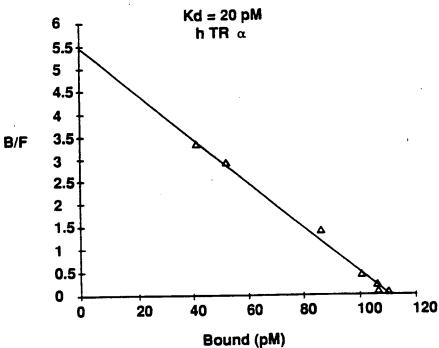
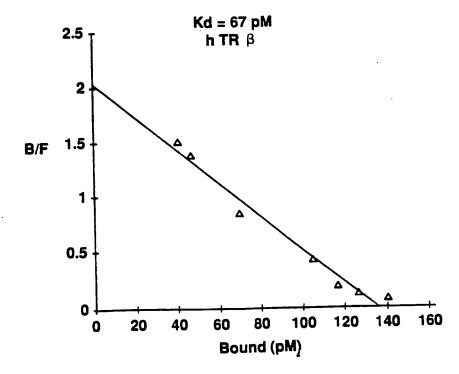
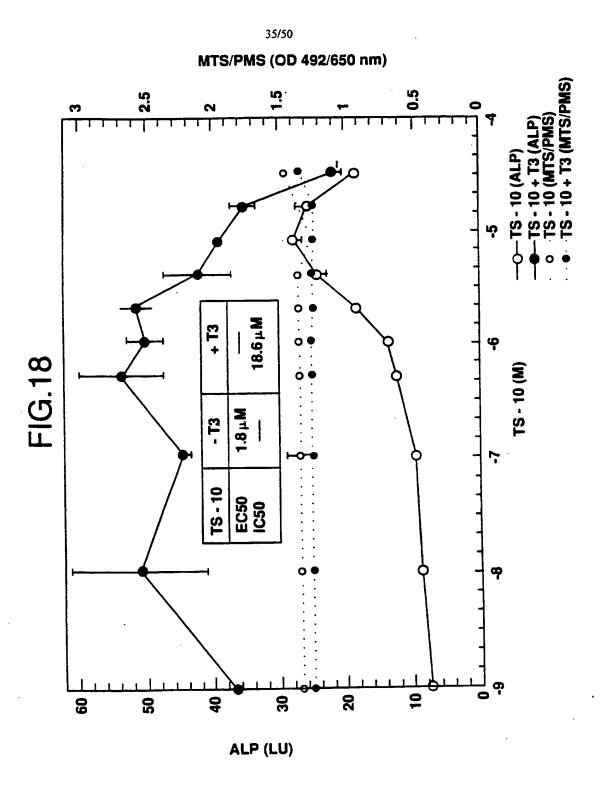


FIG.17B

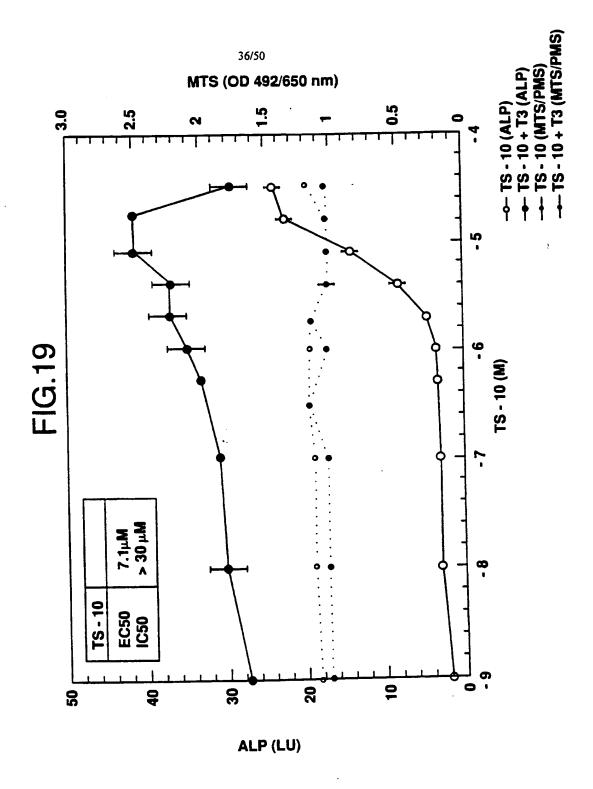


SUBSTITUTE SHEET (RULE 26)

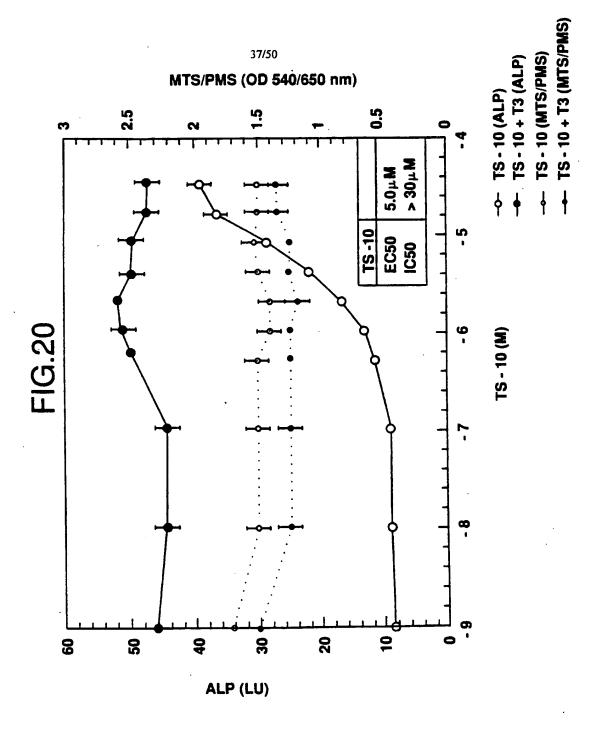


SUBSTITUTE SHEET (RULE 26)

PCT/US98/25296



PCT/US98/25296



PCT/US98/25296

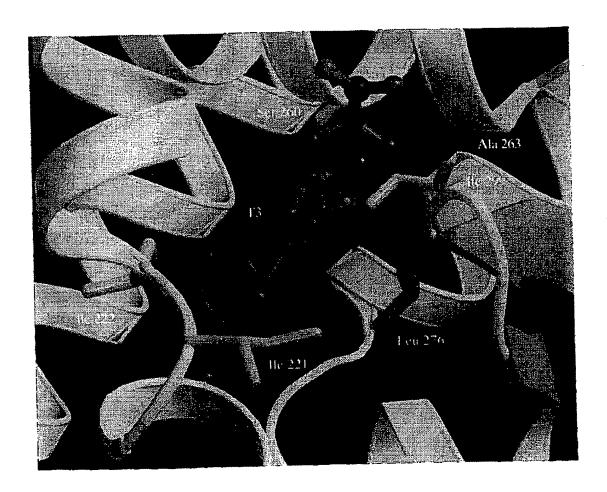


FIG. 21

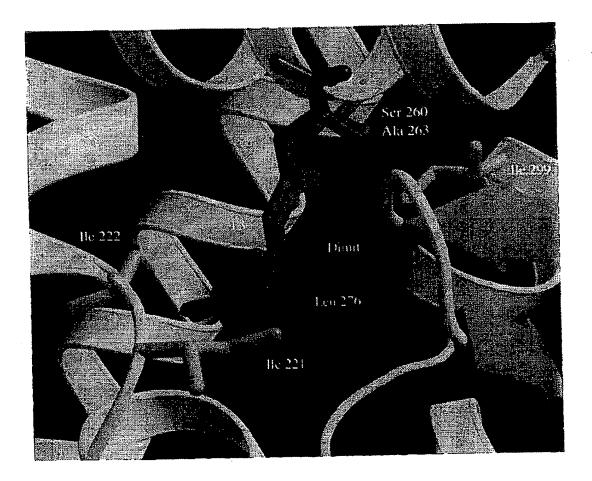


FIG. 22

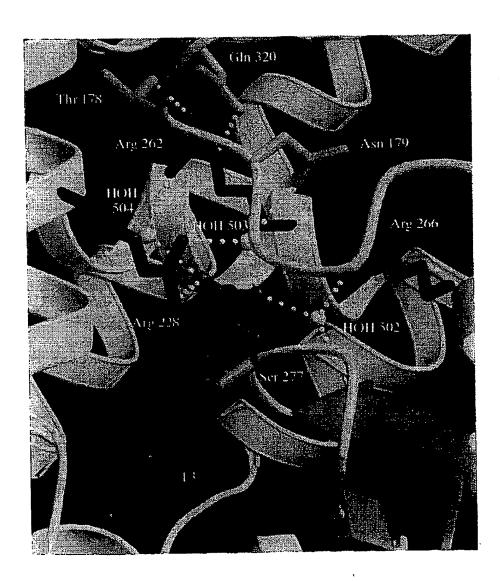


FIG. 23

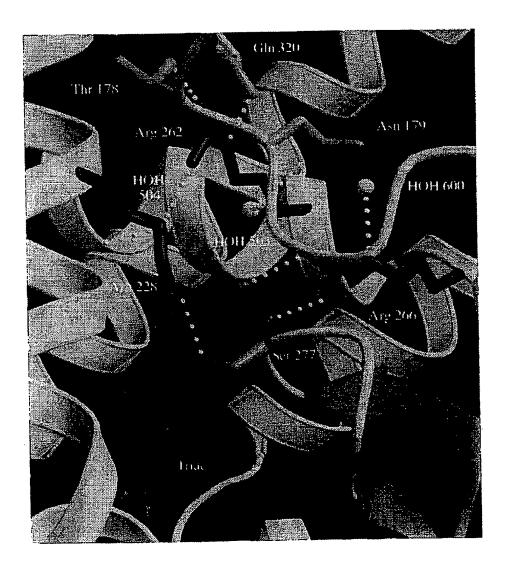


FIG. 24

PCT/US98/25296

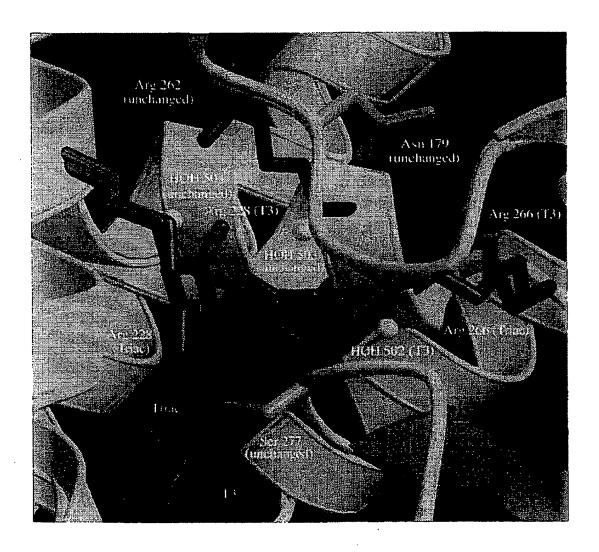


FIG. 25

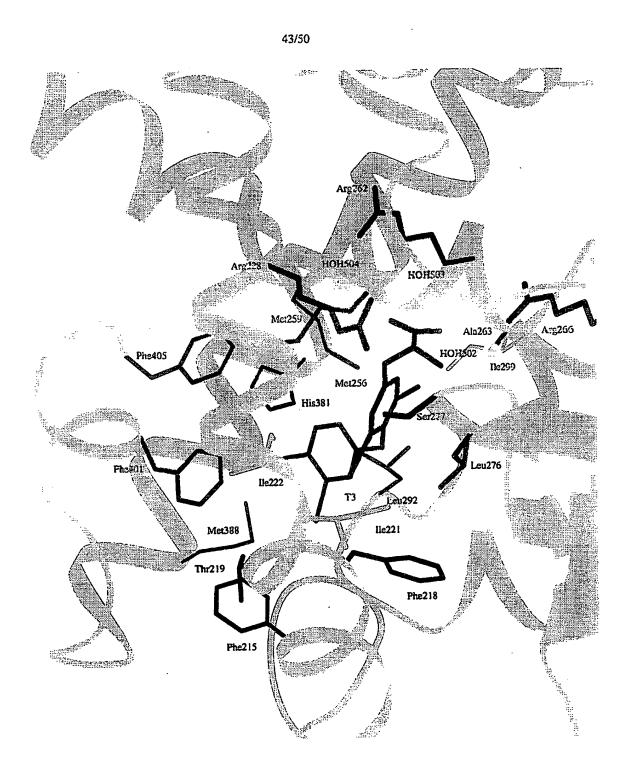


FIG. 26A

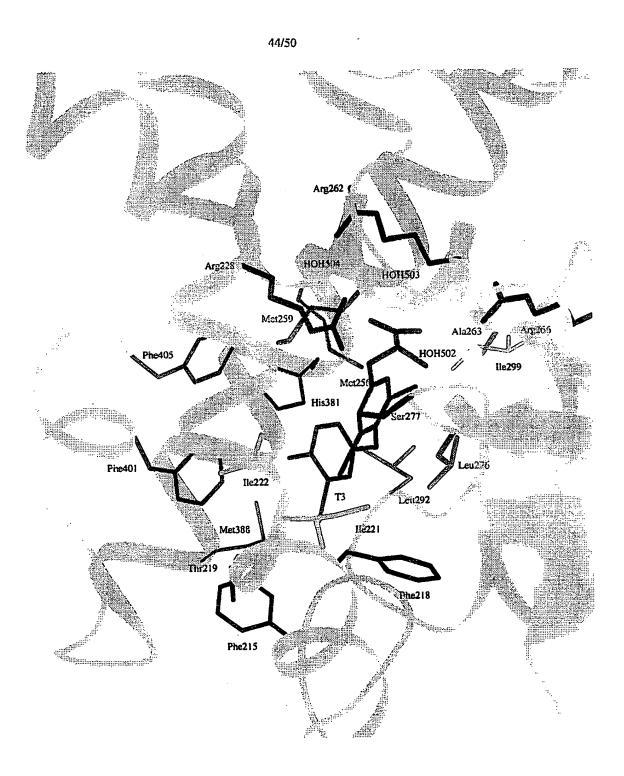


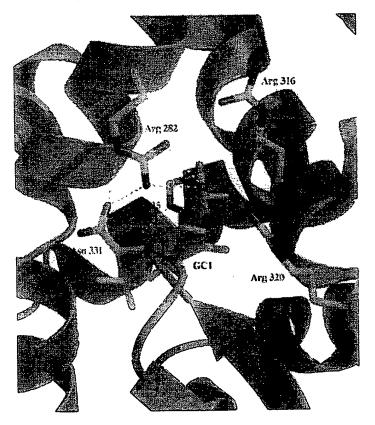
FIG. 26B

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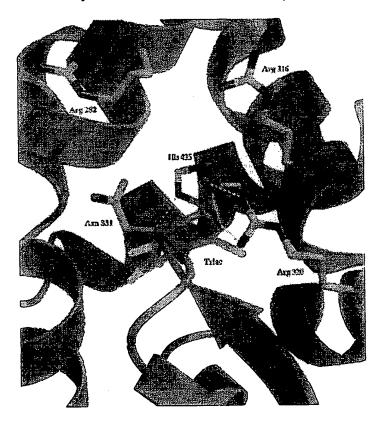
Thyroid Hormone Receptor Beta with GC1



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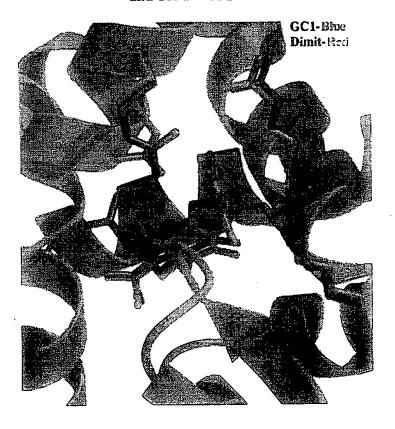
Thyroid Hormone Receptor Beta with Triac



PCT/US98/25296

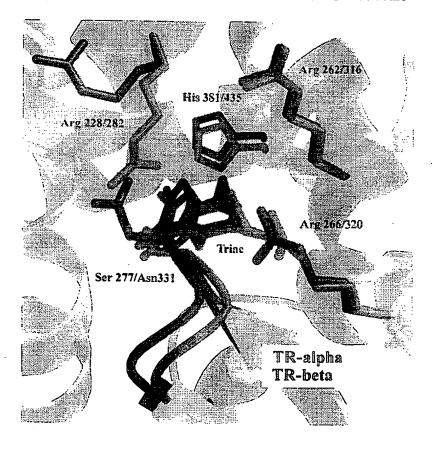
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Structural Differences Between TR-b with GC1 and TR-a with Dimit



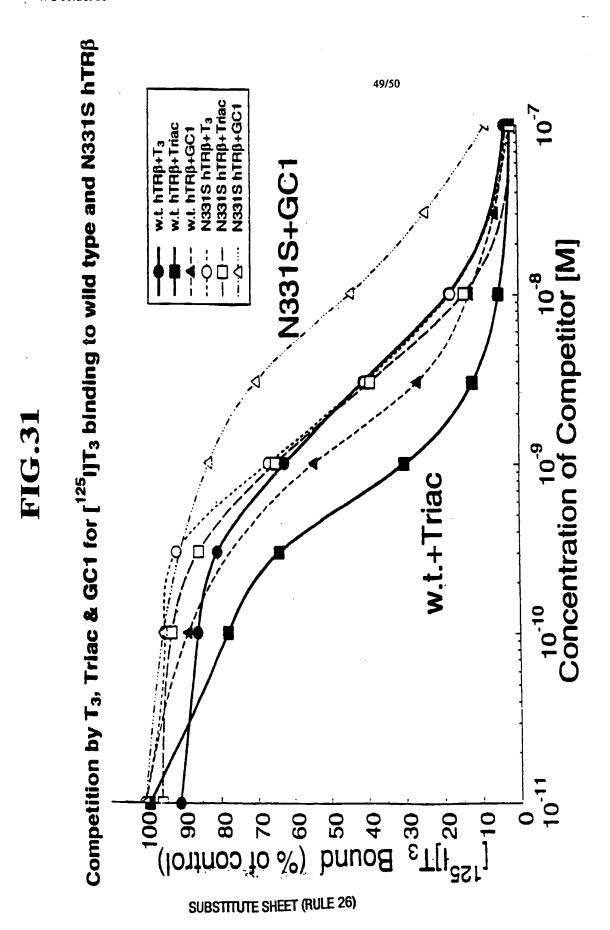
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Structural Differences between TR LBD isoforms with Triac



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Atomic Numbering for Thyronine-like Ligands

Ligand	R1	R3	R5	X	R3'	R4'
Dimit	amino propionic	C19	C20	02	iPr	01
IpBr ₂	amino propionic	BR1	BR2	02	iPr	01
Ť,	amino propionic	I1	I3	O2	12	01
Triac	acetic acid	I1	13	02	12	01
GC1	oxyacetic acid	C19	C20	C21	iPr	O 1

FIG.32